



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 123038

TO: Rei-Tsang Shiao
Location: 5a10 / 5c18
Wednesday, May 26, 2004
Art Unit: 1626
Phone: 272-9797
Serial Number: 10 / 629865

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes



SCIENTIFIC AND TECHNICAL INFORMATION CENTER

Requester's Full Name: Robert (Randy) Shion Examiner #: 7952 Date: 5/26/04
 Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/629865
 Mail Box and Bldg Room Location: Rm 5A101-18 Results Format Preferred (type): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Process for producing (3R-53)
Inventors (please provide full names): Yokubama et al

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

7. search a process for making opd IV by

Formula (I)
or
Formula (II)
or
Formula (III)

+ cell
microorganism
—————→
reducing

Cpd IV

II family (I) $\begin{matrix} \nearrow & (II') \\ \searrow & (III') \end{matrix}$ see figs 2-3

STAFF USE ONLY

Searcher: Jan
 Searcher Phone # 22504
 Searcher Location _____
 Date Searcher Picked Up. 5/26
 Date Completed: 5/26
 Searcher Prep & Review Time: _____
 Clerical Prep Time 10
 Online Time 130

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) ☒ _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other: _____

Vendors and cost where applicable

STN _____

Dialog _____

Questel/Orbit _____

Dr.Link _____

Lexis/Nexis _____

Sequence Systems _____

WWW/Internet _____

Other (specify) _____

=> fil reg

FILE 'REGISTRY' ENTERED AT 15:46:04 ON 26 MAY 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 MAY 2004 HIGHEST RN 685826-98-6

DICTIONARY FILE UPDATES: 25 MAY 2004 HIGHEST RN 685826-98-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

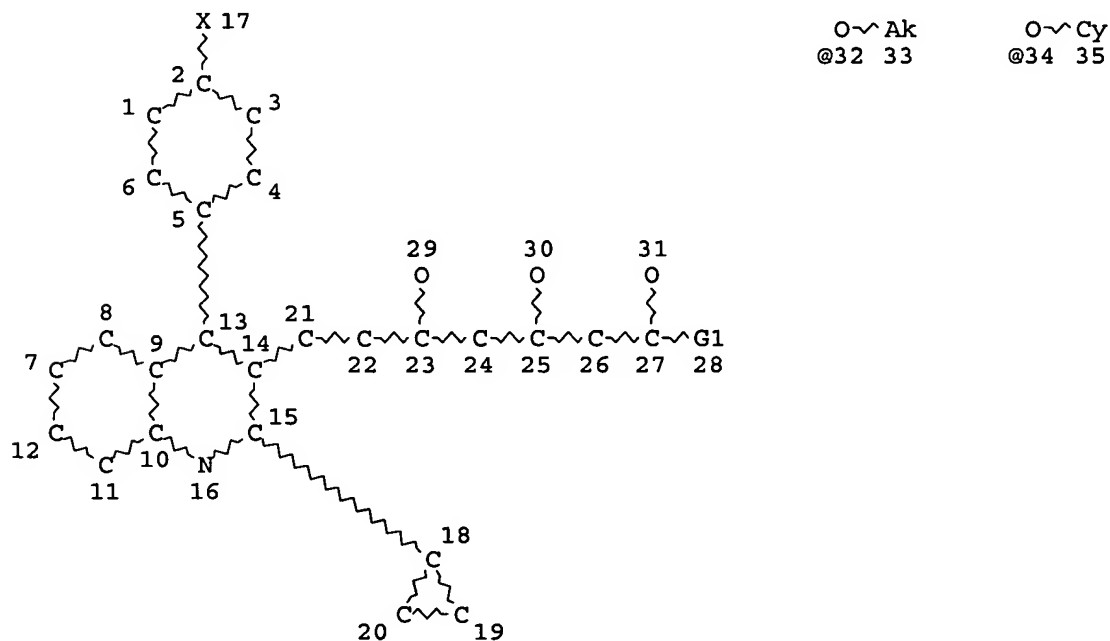
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l3

L1 STR



VAR G1=OH/32/34

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 35

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L3 74 SEA FILE=REGISTRY CSS FUL L1

100.0% PROCESSED 374 ITERATIONS
SEARCH TIME: 00.00.01

74 ANSWERS

=> d his

(FILE 'HOME' ENTERED AT 15:17:47 ON 26 MAY 2004)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 15:17:57 ON 26 MAY 2004

L1 STR
L2 3 S L1 CSS
L3 74 S L1 CSS FUL
SAV L3 SHIAO629/A TEMP

FILE 'HCAOLD' ENTERED AT 15:21:03 ON 26 MAY 2004

L4 0 S L3

FILE 'HCAPLUS' ENTERED AT 15:21:07 ON 26 MAY 2004

L5 233 S L3
L6 1 S US20040030139/PN OR (WO2002-JP835 OR JP2001-331480 OR JP2001-
E HARA M/AU
L7 412 S E3,E19
E TAKUMA Y/AU
L8 91 S E3,E17,E21
E KATSURADA M/AU
L9 39 S E3,E5
E HOSOKAWA A/AU
L10 33 S E3,E4
E MATSUMOTO Y/AU
L11 489 S E3
E MATSUMOTO YOU/AU
L12 14 S E4
E KASUGA Y/AU
L13 50 S E3,E33
E WATANABE N/AU
L14 595 S E3,E4,E62
L15 1 S L5 AND L6
L16 2 S L5 AND L7-L14
L17 2 S L15,L16
L18 34 S L5 AND (MITSUBISHI? OR NISSAN?)/PA,CS
L19 2 S L17 AND L18
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 15:26:50 ON 26 MAY 2004

L20 10 S E1-E10

FILE 'HCAPLUS' ENTERED AT 15:28:17 ON 26 MAY 2004

L21 111 S L5 AND (PD<=20010202 OR PRD<=20010202 OR AD<=20010202)
L22 39 S L3(L) PREP+NT/RL
L23 39 S L3/P
L24 21 S L21 AND L22,L23
E MICROORGANISM/CW
L25 1 S E3,E4,E5 AND L21
E MICROORGANISM/CT
E E3+ALL
L26 1 S E3,E4,E2+NT AND L21
L27 1 S L25,L26
L28 3 S L22,L23 AND ?MICROORG?
L29 3 S L27,L28
E METSCHNIKOWIA/CT

L30 1 S E3+OLD,NT,PFT AND L21
 E CRYPTOCOCCUS/CT
 E E3+ALL
 L31 1 S L21 AND (E1+OLD,NT,PFT OR E2+OLD,NT,PFT OR E3+OLD,NT,PFT)
 E CANDIDA/CT
 L32 1 S E3+OLD,NT,PFT AND L21
 E FILOBASIDIUM/CT
 L33 1 S E3+OLD,NT,PFT AND L21
 E OGATAEA/CT
 L34 1 S E3+OLD,NT,PFT AND L21
 E CITEROMYCES/CT
 L35 1 S E3+OLD,NT,PFT AND L21
 L36 1 S E4+OLD,NT,PFT AND L21
 L37 0 S E5+OLD,NT,PFT AND L21
 E YARROWIA/CT
 L38 1 S E3+OLD,NT,PFT AND L21
 L39 1 S E5+OLD,NT,PFT AND L21
 E RHODOTORULA/CT
 L40 1 S E3+OLD,NT,PFT AND L21
 E EXOPHIALA/CT
 L41 1 S E3+OLD,NT,PFT AND L21
 E TRIGONOPSIS/CT
 L42 1 S E3+OLD,NT,PFT AND L21
 L43 1 S E4+OLD,NT,PFT AND L21
 E SHIZOSACCHAROMYCES/CT
 E SCHIZOSACCHAROMYCES/CT
 L44 1 S E3+OLD,NT,PFT AND L21
 E WICKERHAMIELLA/CT
 L45 1 S E3+OLD,NT,PFT AND L21
 E PICHIA/CT
 L46 1 S E3+OLD,NT,PFT AND L21
 E SACCHAROMYCOPSIS/CT
 L47 1 S E3+OLD,NT,PFT AND L21
 E SAITOELLA/CT
 L48 1 S E3+OLD,NT,PFT AND L21
 E SACCHAROMYCES/CT
 L49 1 S E3+OLD,NT,PFT AND L21
 E RHODOSPORIDIUM/CT
 L50 1 S E3+OLD,NT,PFT AND L21
 E ACINETOBACTER/CT
 L51 1 S E3+OLD,NT,PFT AND L21
 E BREVIBACTERIUM/CT
 L52 1 S E3+OLD,NT,PFT AND L21
 E CELLULOMONAS/CT
 L53 1 S E3+OLD,NT,PFT AND L21
 E CORYNEBACTERIUM/CT
 L54 1 S E3+OLD,NT,PFT AND L21
 E CURTOBACTERIUM/CT
 L55 1 S E3+OLD,NT,PFT AND L21
 L56 3 S L19,L25-L55
 L57 3 S L56 AND L5-L19,L21-L56
 L58 1 S L5 AND (BREVIBACTER? OR CELLULOMON? OR CORYNEBACTER? OR CURTO
 L59 10 S L5 AND (METSCHNIKOW? OR CRYPTOCOC? OR CANDIDA? OR FILOBASID?
 L60 10 S L19,L25-L59
 L61 2 S L60 AND L21
 L62 3 S L19,L61
 L63 7 S L60 NOT L62
 L64 1 S L63 AND MICROORGANISM
 L65 4 S L62,L64

FILE 'REGISTRY' ENTERED AT 15:45:10 ON 26 MAY 2004

FILE 'HCAPLUS' ENTERED AT 15:45:19 ON 26 MAY 2004

L66

3 S L65 NOT ITAVASTATIN

FILE 'REGISTRY' ENTERED AT 15:46:04 ON 26 MAY 2004

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 15:46:11 ON 26 MAY 2004

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FILE COVERS 1907 - 26 May 2004 VOL 140 ISS 22

FILE LAST UPDATED: 25 May 2004 (20040525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 166

L66 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:757860 HCAPLUS

DN 139:272910

ED Entered STN: 26 Sep 2003

TI Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcohols

IN Hiraoka, Hirotoshi; Ueda, Makoto; Hara, Mari

PA Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

IC ICM C12N015-53

ICS C12N009-04; C12N001-21; C12P017-02; C12P041-00; C12R001-645; C12R001-19

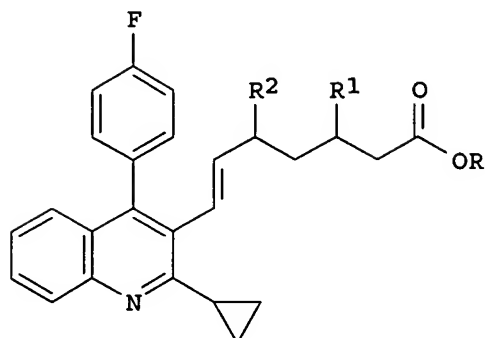
CC 7-2 (Enzymes)

Section cross-reference(s): 3, 10, 16

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003078634	A1	20030925	WO 2003-JP3262	20030318
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

JP 2003339387 A2 20031202 JP 2003-74017 20030318
 PRAI JP 2002-75921 A 20020319
 GI



I

- AB Provide a novel carbonyl reductase originating in a microorganism belonging to the genus *Ogataea*, an encoding gene, recombinant expression, and use for producing optically active alcs. By reducing ketones having general structures I ($R = H$, alkyl, aryl; $R_1 = :O$, OH , $(R)-OH$; $R_2 = OH$, $(S)-OH$, $:O$) with the use of carbonyl reductase, optically active alcs., in particular, (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid esters, can be produced. A novel carbonyl reductase was isolated from *Ogataea minuta* var. nonfermentans strain IFO 1473. Its substrate specificity was investigated with various ketones and aldehydes. Its activity for reduction of 2,2,2-Trifluoroacetophenone was significantly inhibited by $Hg(I)$ ion and $Zn(II)$ ion. Its gene was cloned, sequenced, and expressed in *E. coli*. The recombinant enzyme was used in production of. (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid Et ester (3R,5S-DOLE) from (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid Et ester (DOXE) or 5S-(E)-7-[2-cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohept-6-enoic acid Et ester (5S-MOLE), is described. The yield was 319 μg (31.9% with 100% e.e. optical purity), and 807 μg (80.7% with 97% e.e. optical purity), resp.
- ST carbonyl reductase gene *Ogataea* optically active alc
- IT Asymmetric synthesis and induction
 DNA sequences
 Molecular cloning
Ogataea minuta nonfermentans
 Protein sequences
 (*Ogataea minuta* carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT Alcohols, preparation
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
 (*Ogataea minuta* carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT Gene, microbial
 RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
 (*Ogataea minuta* carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT Reduction
 (enzymic, stereoselective; *Ogataea minuta* carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT Purity
 (optical; *Ogataea minuta* carbonyl reductase, encoding gene, and use for producing optically active alcs.)

- IT Escherichia coli
(recombinant expression in; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT Aldehydes, biological studies
Ketones, biological studies
RL: BCP (Biochemical process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(reduction of; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT 167073-19-0P, (3R,5S)-(E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid ethyl ester
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT 77106-95-7P, Carbonyl reductase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT 22542-11-6, biological studies 23713-49-7, Zinc ion, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reduction of 2,2,2-Trifluoroacetophenone inhibited by; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT 166803-31-2, (E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid ethyl ester 254452-91-0, 5S-(E)-7-[2-Cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohept-6-enoic acid ethyl ester
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(reduction of, substrate; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT 89-98-5, o-Chlorobenzaldehyde 93-55-0, Propiophenone 94-02-0, Ethylbenzoyl acetate 99-02-5, m-Chloroacetophenone 99-61-6, m-Nitrobenzaldehyde 99-91-2, p-Chloroacetophenone 104-88-1, p-Chlorobenzaldehyde, biological studies 431-03-8, Diacetyl 434-45-7, 2,2,2-Trifluoroacetophenone 532-27-4, 2-Chloroacetophenone 552-89-6, o-Nitrobenzaldehyde 587-04-2, m-Chlorobenzaldehyde 600-14-6, 2,3-Pentanedione 645-59-0, Benzylacetone nitrile 822-87-7, 2-Chlorocyclohexanone 1694-29-7, 3-Chloro-2,4-pentadione 2142-63-4, m-Bromoacetophenone 5469-26-1, 1-Bromo-3,3-dimethyl-2-butanone 10409-46-8, 2-Chloro-2-Methylcyclohexanone 13031-04-4 20201-24-5, Ethyl-3-methyl-2-oxobutanoate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reduction of, substrate; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
- IT 606130-03-4 606130-04-5 606130-05-6 606130-06-7
RL: PRP (Properties)
(unclaimed sequence; ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Mitsubishi Chemical Corp; WO 02063028 A1 2002 HCAPLUS
 - (2) Mitsubishi Chemical Corp; JP 2002300897 A 2002 HCAPLUS
 - (3) Nissan Chemical Industries Ltd; JP 01-279866 A 1989 HCAPLUS
 - (4) Nissan Chemical Industries Ltd; EP 304063 A2 1989 HCAPLUS
 - (5) Nissan Chemical Industries Ltd; US 5011930 A 1989 HCAPLUS
 - (6) Nissan Chemical Industries Ltd; JP 08-127585 A 1996 HCAPLUS
 - (7) Nissan Chemical Industries Ltd; JP 08-92217 A 1996 HCAPLUS
- IT 167073-19-0P, (3R,5S)-(E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid ethyl ester
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP

(Preparation)

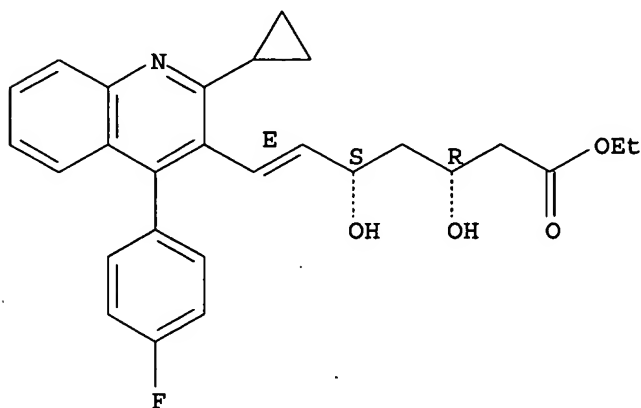
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

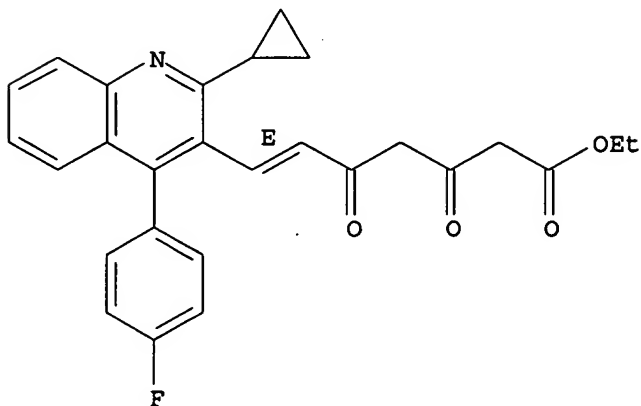


IT 166803-31-2, (E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid ethyl ester 254452-91-0,
5S-(E)-7-[2-Cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohept-6-enoic acid ethyl ester
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(reduction of, substrate; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

RN 166803-31-2 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

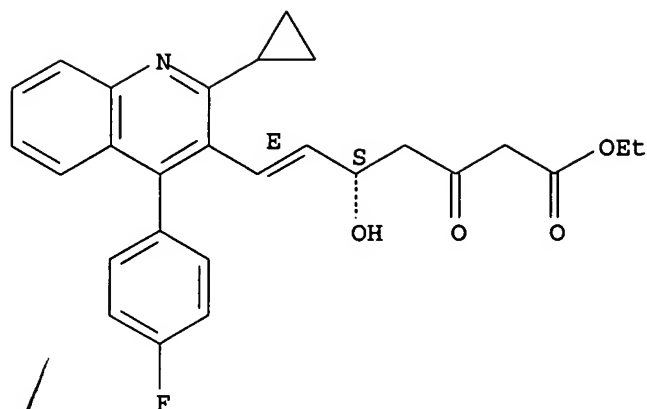


RN 254452-91-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L66 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:663303 HCAPLUS

DN 139:178816

ED Entered STN: 26 Aug 2003

TI Optically active hydroxyketo esters manufacture with **microorganism**

IN Asano, Yasuhisa; Suzuki, Kenji; Matsumoto, Hiroo

PA Nissan Chemical Industries, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM C12P017-12

ICS C12R001-84; C12R001-645; C12R001-865

CC 16-2 (Fermentation and Bioindustrial Chemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2003235595	A2	20030826	JP 2002-38670	20020215
PRAI	JP 2002-38670		20020215		

OS MARPAT 139:178816

AB The title optically active hydroxyketo esters (I) are manufactured by asym. reduction with **microorganism** such as **Saccharomyces cerevisiae**. I, especially

(3R,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3-hydroxy-5-oxy-6-heptanoic acid Et ester, are useful intermediates for manufacture of HMG-CoA reductase inhibitors which are useful for preparing hypocholesteremics.

ST hydroxyketo ester manuf **Saccharomyces microorganism**
hypocholesteremic intermediate

IT Resolution (separation)
(enzymic; optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

IT Anticholesteremic agents
(intermediates for; optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

IT Fermentation
Hansenula wickerhamii
Kuraishia

Ogataea

Pichia

Pichia angusta

Pichia anomala

Pichia capsulata

Pichia farinosa

Pichia naganishii**Saccharomyces****Saccharomyces cerevisiae**

Yamadazyma

(optically active hydroxyketo esters manufacture with **microorganism**
by asym. reduction)

IT Reduction

(stereoselective; optically active hydroxyketo esters manufacture with
microorganism by asym. reduction)

IT 444732-68-7P

RL: BPN (Biosynthetic preparation); BIOL (Biological study);

PREP (Preparation)

(optically active hydroxyketo esters manufacture with **microorganism**
by asym. reduction)

IT 166803-31-2

RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological
study); RACT (Reactant or reagent)(optically active hydroxyketo esters manufacture with **microorganism**
by asym. reduction)

IT 444732-68-7P

RL: BPN (Biosynthetic preparation); BIOL (Biological study);

PREP (Preparation)

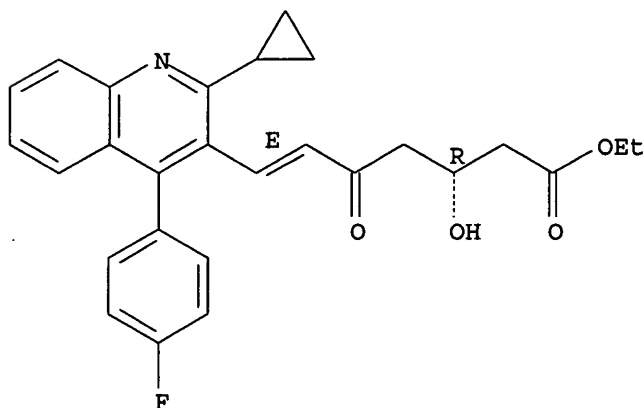
(optically active hydroxyketo esters manufacture with **microorganism**
by asym. reduction)

RN 444732-68-7 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-
hydroxy-5-oxo-, ethyl ester, (3R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



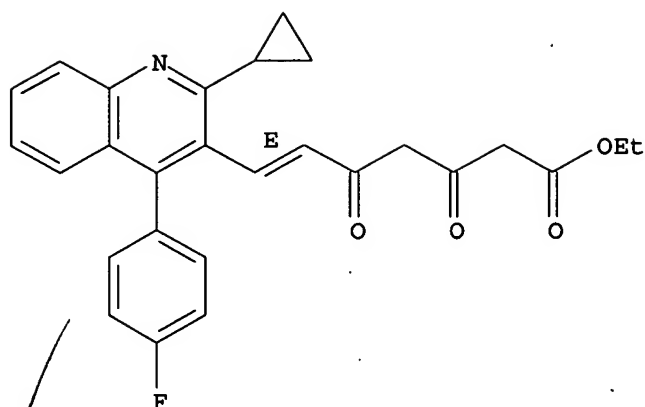
IT 166803-31-2

RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological
study); RACT (Reactant or reagent)(optically active hydroxyketo esters manufacture with **microorganism**
by asym. reduction)

RN 166803-31-2 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L66 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:615881 HCAPLUS

DN 137:139496

ED Entered STN: 16 Aug 2002

TI Process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivatives

IN Hara, Mari; Takuma, Yuki; Katsurada, Manabu;

Hosokawa, Akemi; Matsumoto, Youichi; Kasuga,

Yuzo; Watanabe, Naoyuki

PA Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.

SO PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

IC ICM C12P017-12

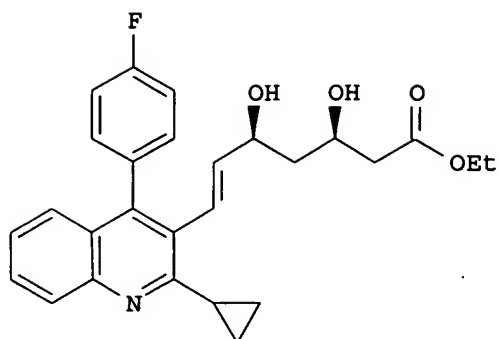
ICS C12P017-12; C12R001-645

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002063028	A1	20020815	WO 2002-JP835	20020201 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	JP 2003137870	A2	20030514	JP 2001-331480	20011029 <--
	JP 2002300897	A2	20021015	JP 2002-25423	20020201 <--
	EP 1365029	A1	20031126	EP 2002-710461	20020201 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	US 2004030139	A1	20040212	US 2003-629865	20030730 <--
PRAI	JP 2001-26316	A	20010202	<--	
	JP 2001-331480	A	20011029	<--	
	WO 2002-JP835	W	20020201	<--	
OS	CASREACT 137:139496; MARPAT 137:139496				
GI					



I

- AB A process for producing the title compound (I) and optically active derivs. with **microorganism** by fermentation was given. I is useful as serum cholesterol-reducing agent. Preparation of Et ester of I (3R,5S-DOLE) and its derivs. 3S,5R-, 3S,5S-, and 3R,5R-DOLE with **Saccharomycopsis fibuligera** from 5-Mol, i.e. 5-(E)-7-[2-cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohept-6-enoic acid Et ester was shown.
- ST DOLE serum cholesterol reducing agent fermn **microorganism**; deriv DOLE fermn **microorganism** **Saccharomycopsis**
- IT Reduction
(biochem., stereoselective; process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)
- IT Reduction
(enzymic, stereoselective; process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)
- IT Resolution (separation)
(enzymic; process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)
- IT **Acinetobacter**
Acinetobacter calcoaceticus
Anticholesteremic agents
Brevibacterium
Brevibacterium saccharolyticum
Candida
Candida albicans
Candida cylindracea
Candida famata
Candida famata famata
Candida intermedia
Candida molischiana
Candida parapsilosis
Candida solani
Candida tropicalis
Cellulomonas
Cellulomonas flavigena
Cellulomonas gelida
Cellulomonas uda
Citeromyces
Citeromyces matritensis
Corynebacterium
Corynebacterium acetoacidophilum
Corynebacterium ammoniagenes
Corynebacterium glutamicum
Corynebacterium vitaeruminis
Cryptococcus (fungus)

Cryptococcus curvatus
 Cryptococcus flavus
 Cryptococcus humicolus
 Cryptococcus laurentii
 Curtobacterium
 Curtobacterium flaccumfaciens

Drugs

Exophiala
 Exophiala dermatitidis

Fermentation

Filobasidium
 Filobasidium capsuligenum
 Metschnikowia
 Metschnikowia bicuspidata
 Metschnikowia pulcherrima
 Metschnikowia reukaufii
 Microorganism
 Ogataea
 Ogataea minuta
 Ogataea minuta nonfermentans
 Pichia
 Pichia anomala
 Pichia glucozyma
 Pichia petersonii
 Rhodosporidium
 Rhodosporidium toruloides
 Rhodotorula
 Rhodotorula aurantiaca
 Rhodotorula mucilaginosa
 Saccharomyces
 Saccharomyces cerevisiae
 Saccharomycopsis
 Saccharomycopsis fibuligera
 Saitoella
 Saitoella complicata
 Schizosaccharomyces
 Schizosaccharomyces pombe
 Trigonopsis
 Trigonopsis variabilis
 Wickerhamiella
 Wickerhamiella domercquii
 Yarrowia
 Yarrowia lipolytica

(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT 148901-69-3 166803-31-2 444732-67-6
 444732-68-7

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);
 PROC (Process); RACT (Reactant or reagent)

(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT 147511-69-1P 167073-18-9P 167073-19-0P
 380848-30-6P 380848-32-8P

RL: BPN (Biosynthetic preparation); BIOL (Biological study);
 PREP (Preparation)

(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) E R Squibb & Sons Inc; CA 2094191 A 1993 HCAPLUS
- (2) E R Squibb & Sons Inc; US 5324662 A 1993 HCAPLUS
- (3) E R Squibb & Sons Inc; EP 569998 A2 1993 HCAPLUS
- (4) E R Squibb & Sons Inc; JP 630783 A 1993

- (5) Nagamatsu, S; J Chromatogr A 1999, V832, P55 HCAPLUS
- (6) Nissan Chemical Industries Ltd; JP 01279866 A 1989 HCAPLUS
- (7) Nissan Chemical Industries Ltd; EP 304063 A2 1989 HCAPLUS
- (8) Nissan Chemical Industries Ltd; US 5011930 A 1989 HCAPLUS
- (9) Nissan Chemical Industries Ltd; US 5102888 A 1989 HCAPLUS
- (10) Nissan Chemical Industries Ltd; US 5185328 A 1989 HCAPLUS
- (11) Nissan Chemical Industries Ltd; US 5854259 A 1989 HCAPLUS
- (12) Nissan Chemical Industries Ltd; US 5856336 A 1989 HCAPLUS
- (13) Nissan Chemical Industries Ltd; US 5872130 A 1989 HCAPLUS
- (14) Ube Industries Ltd; JP 08127585 A 1996 HCAPLUS
- (15) Ube Industries Ltd; JP 892217 A 1996

IT 148901-69-3 166803-31-2 444732-67-6

444732-68-7

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);

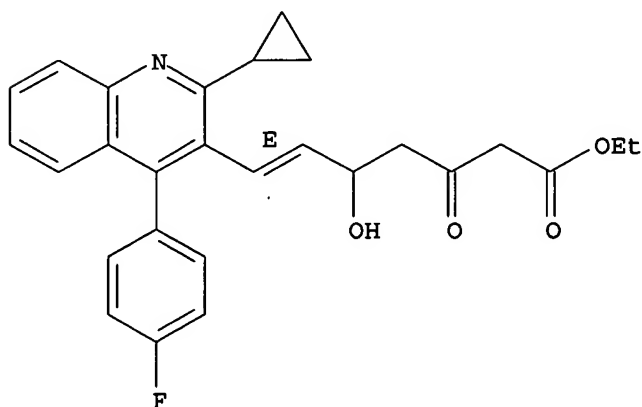
PROC (Process); RACT (Reactant or reagent)

(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

RN 148901-69-3 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)-(9CI) (CA INDEX NAME)

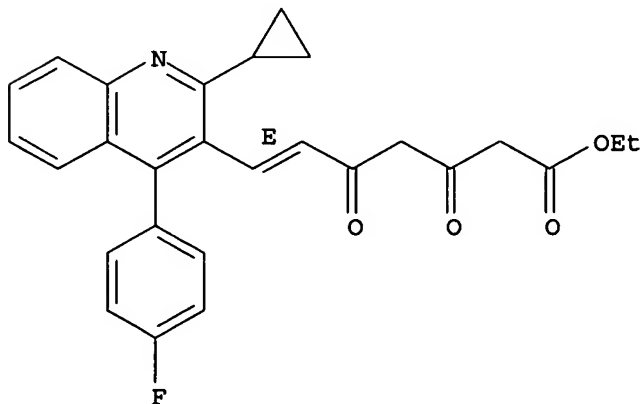
Double bond geometry as shown.



RN 166803-31-2 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)-(9CI) (CA INDEX NAME)

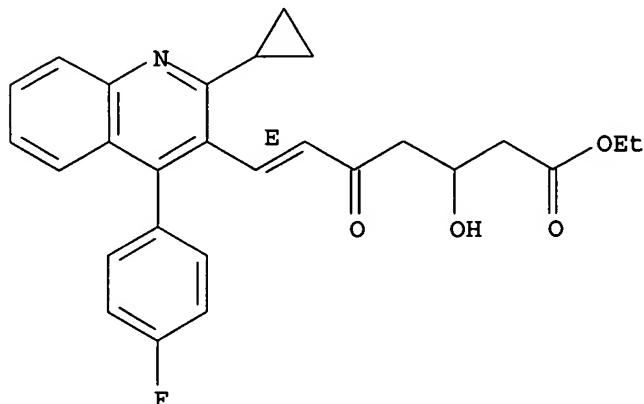
Double bond geometry as shown.



RN 444732-67-6 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

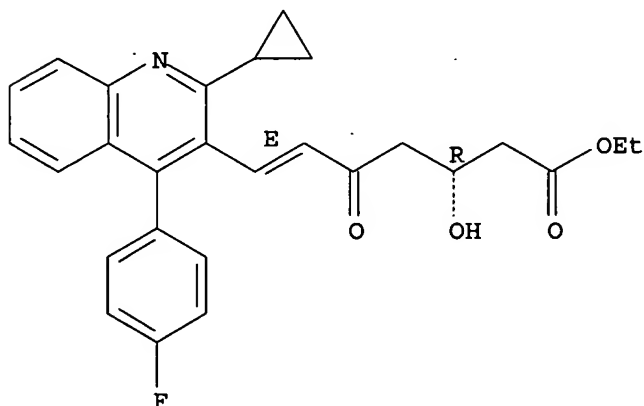


RN 444732-68-7 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, ethyl ester, (3R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 147511-69-1P 167073-18-9P 167073-19-0P

380848-30-6P 380848-32-8P

RL: BPN (Biosynthetic preparation); BIOL (Biological study);

PREP (Preparation)

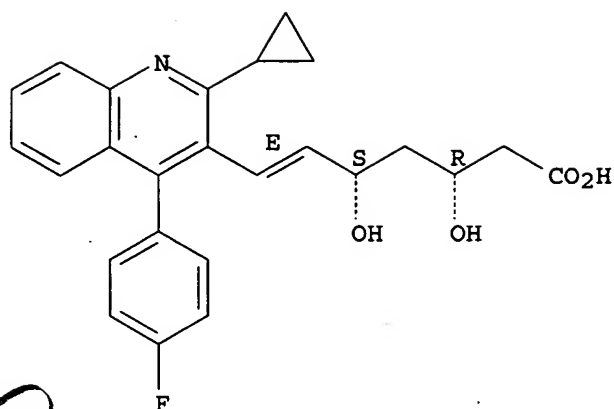
(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

RN 147511-69-1 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

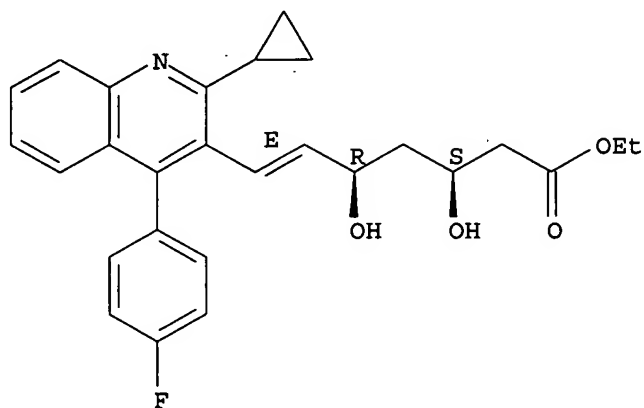
Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



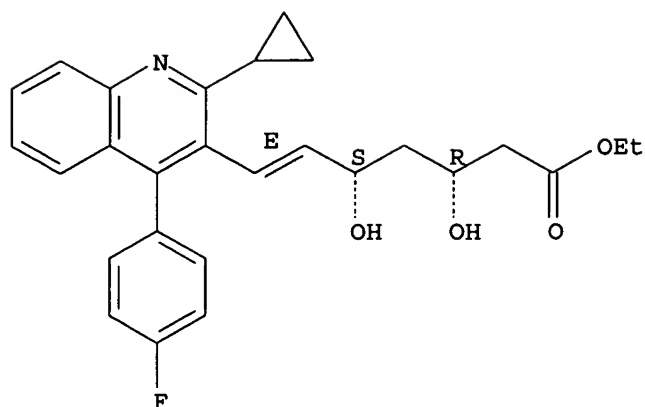
RN 167073-18-9 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 167073-19-0 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

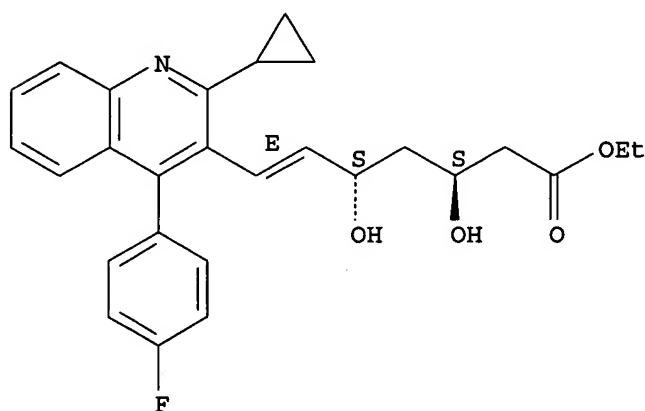
Absolute stereochemistry.
 Double bond geometry as shown.



RN 380848-30-6 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5S,6E)- (9CI) (CA INDEX NAME)

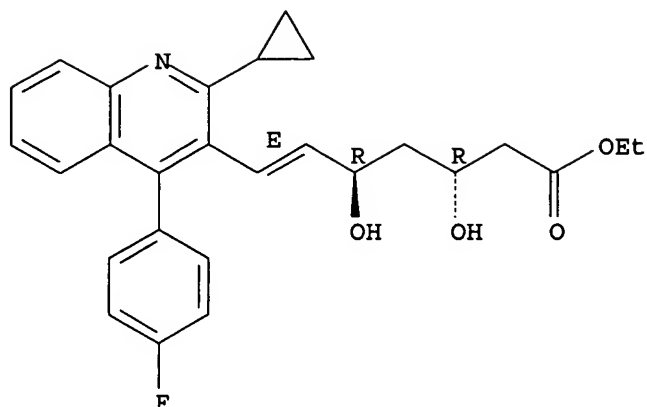
Absolute stereochemistry.
Double bond geometry as shown.



RN 380848-32-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



=> => d his l67

(FILE 'REGISTRY' ENTERED AT 15:46:04 ON 26 MAY 2004)

FILE 'HCAPLUS' ENTERED AT 15:46:11 ON 26 MAY 2004

L67 20 S L24 NOT L66

=> d bib abs hitstr tot

L67 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:154436 HCAPLUS

DN 138:204870

TI Processes for preparing calcium salt forms of statins

IN Niddam-Hildesheim, Valerie; Lifshitz-Liron, Revital; Lidor-Hadas, Rami

PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

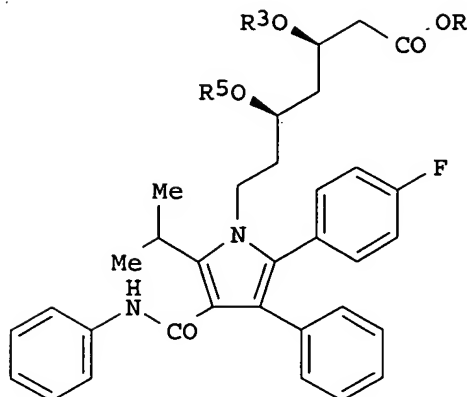
DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003016317	A1	20030227	WO 2002-US26012	20020816
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				
	PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				
	UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,				
	RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,				
	CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				
	PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,				
	NE, SN, TD, TG				
	US 2002099224	A1	20020725	US 2001-37412	20011024 <--
	US 6528661	B2	20030304		
	US 2003114685	A1	20030619	US 2002-222556	20020816
PRAI	US 2001-312812P	P	20010816		
	US 2001-37412	A	20011024		
	US 2000-249319P	P	20001116	<--	
	US 2001-312144P	P	20010813		
	US 2001-326529P	P	20011001		

OS MARPAT 138:204870
GI



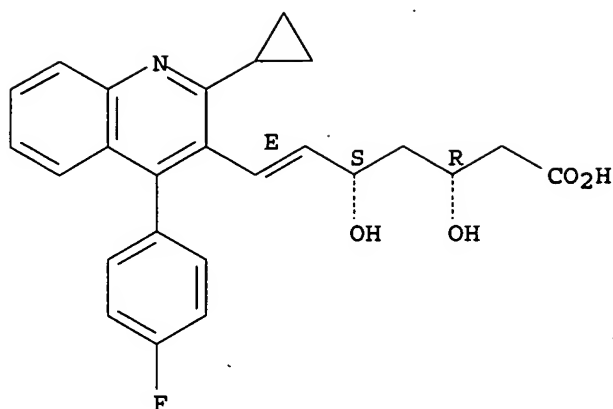
I

AB Processes for preparing hemicalcium salts of a statins
 $\text{RCH(OH)CH}_2\text{CH(OH)CH}_2\text{CO}_2\text{H}$ (R = statin organic radical selected from pravastatin, fluvastatin, cerivastatin, atorvastatin, rosuvastatin, pitavastatin, simvastatin, or lovastatin) from an ester derivative or protected ester derivative of the statin by using calcium hydroxide are provided. The ester or protected ester derivative is contacted with calcium hydroxide to obtain the calcium salt. Preferred statins are rosuvastatin, pitavastatin and atorvastatin, simvastatin and lovastatin. In processes beginning with a protected statin ester derivative, the protecting group is hydrolyzed during salt formation by contact with calcium hydroxide, or is contacted with an acid catalyst followed by contact with calcium hydroxide. Thus, diol-protected atorvastatin ester I (R = CMe₃, R₃R₅ = CMe₂) was treated with an 80% aqueous soln of AcOH at rt for 20 h to form the deprotected ester I (R = CMe₃, R₃ = R₅ = H) which was in turn dissolved in EtOH, treated with a saturated soln of Ca(OH)₂ containing Bu₄N⁺Br⁻ and stirred at 45° for 24 h to give atorvastatin hemicalcium salt I (R = 1/2Ca, R₃ = R₅ = H) in 77% yield for the two steps.

IT 147526-32-7P, Pitavastatin hemicalcium
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (processes for preparing calcium salt forms of statins)

RN 147526-32-7 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



● 1/2 Ca

IT 167073-19-0

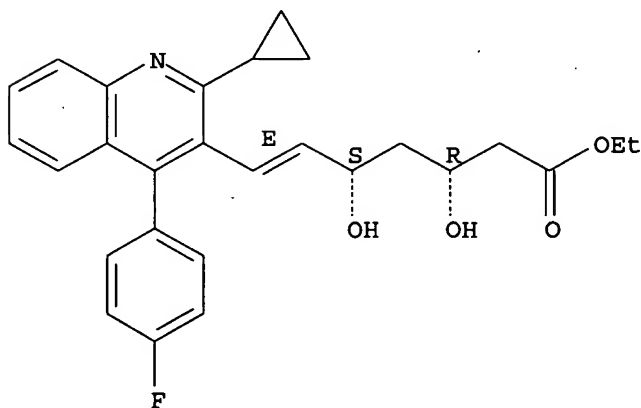
RL: RCT (Reactant); RACT (Reactant or reagent)
(processes for preparing calcium salt forms of statins)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:293628 HCAPLUS

DN 136:325435

TI Process for producing optically active ethyl (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate

IN Onishi, Atsushi; Murazumi, Koichi; Tachibana, Kozo

PA Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.

SO PCT Int. Appl., 30 pp.

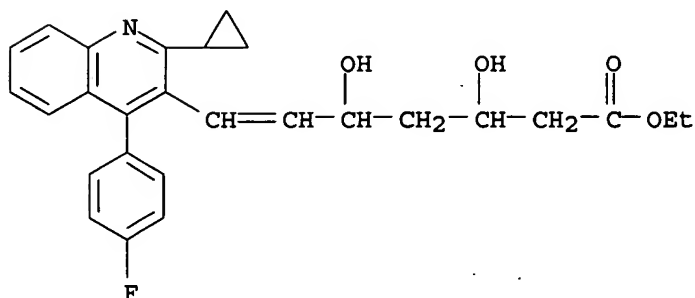
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002030903	A1	20020418	WO 2001-JP9000	20011012 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2001095926	A5	20020422	AU 2001-95926	20011012 <--
	EP 1334967	A1	20030813	EP 2001-976679	20011012 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	JP 2000-314245	A	20001013 <--		
	WO 2001-JP9000	W	20011012		
AB	The process for producing an optically active isomer of Et 7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate comprises optically resolving, at a high efficiency, a mixture of optical isomers of the compound, characterized in that a packing comprising a support and cellulose tris(4-chlorophenylcarbamate) deposited thereon in a specific proportion is used to chromatog. isolate the target isomer under such conditions as to result in a specific retention volume The title compound is an intermediate for the known hypolipemic NK 104.				
IT	121661-13-0 RL: ANT (Analyte); ANST (Analytical study) (process for producing optically active Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate)				
RN	121661-13-0 HCAPLUS				
CN	6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)				



IT 167073-19-0P

RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)

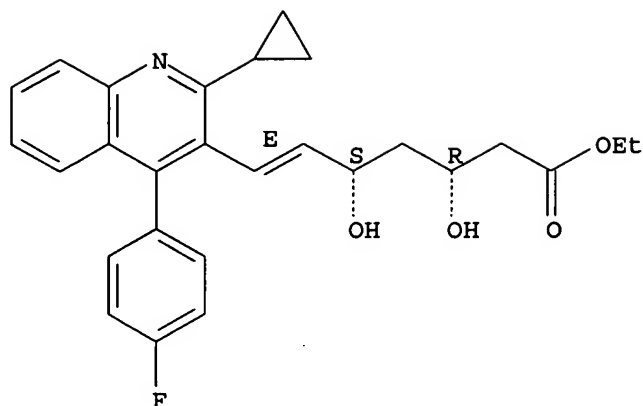
(process for producing optically active Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

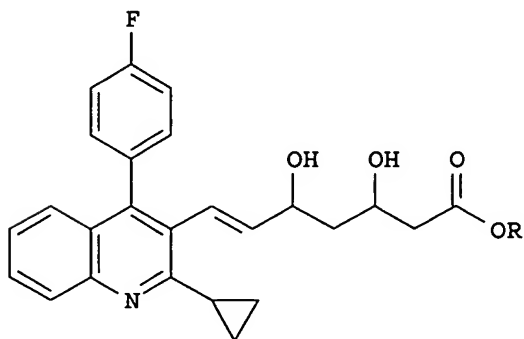
Double bond geometry as shown.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:932409 HCAPLUS
DN 136:36497
TI Manufacture of (3R,5S,6E)-7-(substituted-quinolyl)-3,5-dihydroxyhept-6-
enoic acid esters by stereoselective enzymic hydrolysis
IN Tokuda, Shinichiro; Okabe, Toshiyuki; Soma, Tamotsu
PA Nissan Chemical Industries, Ltd., Japan; Sankyo Kasei Kogyo K. K.
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001352996	A2	20011225	JP 2000-175316	20000612 <--
PRAI	JP 2000-175316		20000612	<--	
OS	MARPAT 136:36497				
GI					



I

AB The compds. (3R,5S,6E)-I (R = C1-4 alkyl) (II), useful as intermediates for (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-dihydroxyhept-6-enoic acid salts as hypolipemics and antiatherosclerotics, are manufactured by treating a mixture of stereoisomers of (6E)-I including II with acylating agents in the presence of hydrolases, removing the hydrolases from the reaction mixture, and then separating II from the mixture

A

mixture (3.37 g) of II (R = Et) 49.7, (3S,5R,6E)-I (R = Et) 49.7, (3S,5S,6E)-I (R = Et) <0.3, and (3R,5R,6E)-I (R = Et) <0.3% was treated with isopropenyl acetate and Lipase PS in Me₃COMe at 40° for 94 h to give 1.40 g II (R = Et) with 99.4% e.e.

IT 147511-69-1DP, salts

RL: PNU (Preparation, unclassified); PREP (Preparation)

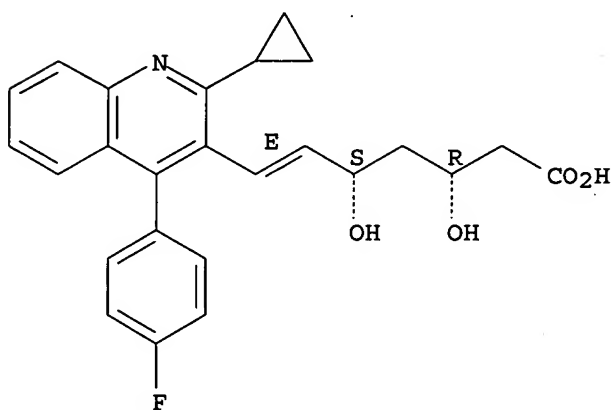
(hypolipemics, intermediates for; manufacture of optically-active quinolyldihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)

RN 147511-69-1 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



IT 167073-19-0P

RL: PUR (Purification or recovery); PREP (Preparation)

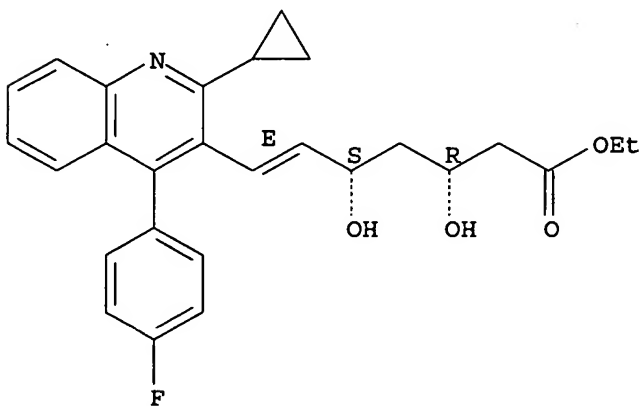
(manufacture of optically-active quinolyldihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 167073-18-9 380848-30-6 380848-32-8

RL: RCT (Reactant); RACT (Reactant or reagent)

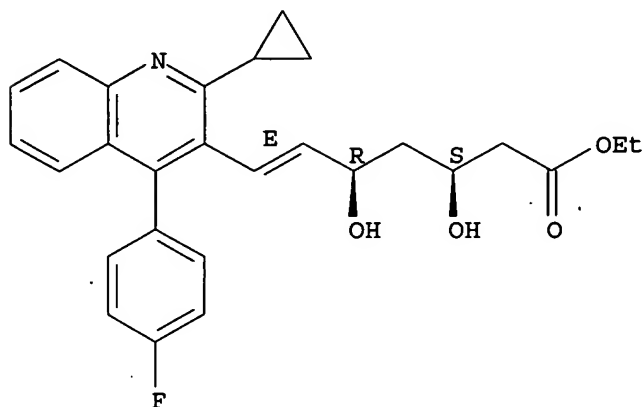
(manufacture of optically-active quinolyldihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)

RN 167073-18-9 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

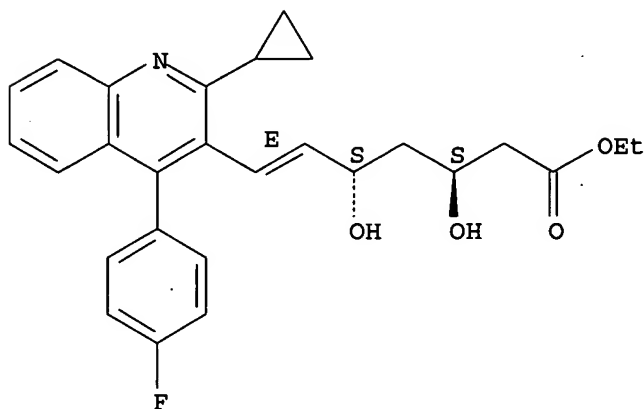


RN 380848-30-6 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

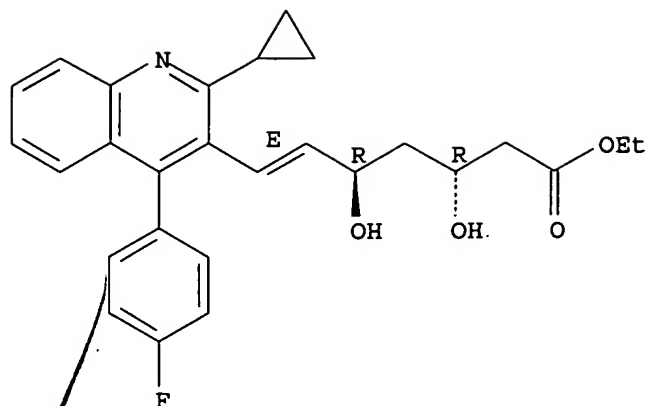


RN 380848-32-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5R,6E)- (9CI) (CA INDEX NAME)

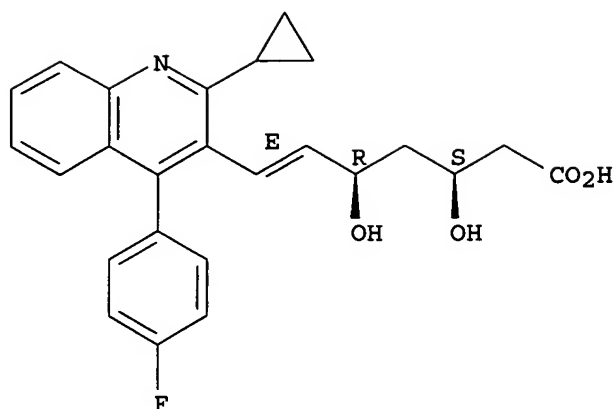
Absolute stereochemistry.

Double bond geometry as shown.



L67 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:667344 HCAPLUS
 DN 136:112193
 TI Synthesis and biological evaluations of quinoline-based HMG-CoA reductase inhibitors
 AU Suzuki, M.; Iwasaki, H.; Fujikawa, Y.; Kitahara, M.; Sakashita, M.; Sakoda, R.
 CS Central Research Laboratories, Nissan Chemical Industries, Ltd., Funabashi, Chiba, 274-8507, Japan
 SO Bioorganic & Medicinal Chemistry (2001), 9(10), 2727-2743
 CODEN: BMECEP; ISSN: 0968-0896
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 AB A series of quinoline-based 3,5-dihydroxyheptenoic acid derivs. were synthesized from quinolinecarboxylic acid esters by homologation, aldol condensation with Et acetoacetate dianion, and reduction of 3-hydroxyketone to evaluate their ability to inhibit the enzyme HMG-CoA reductase in vitro. In agreement with previous literature, a strict structural requirement exists on the external ring, and 4-fluorophenyl is the most active in this system. For the central ring, substitution on positions 6, 7, and 8 of the central quinoline nucleus moderately affected the potency, whereas the alkyl side chain on the 2-position had a more pronounced influence on activity. Among the derivs., NK-104 (pitavastatin calcium), which has a cyclopropyl group as the alkyl side chain, showed the greatest potency. We found that further modulation and improvement in potency at inhibiting HMG-CoA reductase was obtained by having the optimal substituents flanking the desmethylmevalonic acid portion, i.e., 4-fluorophenyl and cyclopropyl, instead of the usual iso-Pr group.
 IT 391681-56-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
 RN 391681-56-4 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

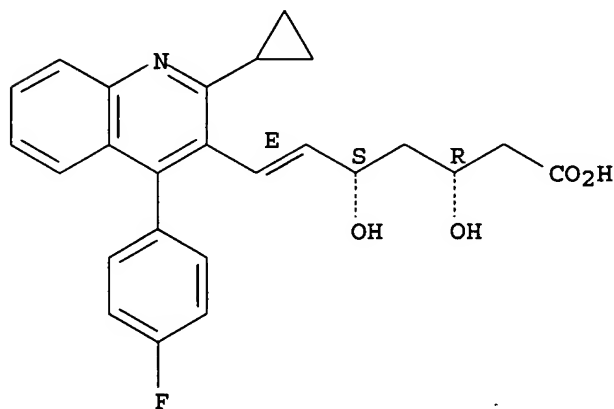
Relative stereochemistry.
 Double bond geometry as shown.



● Na

IT 147526-32-7, NK-104
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
 RN 147526-32-7 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

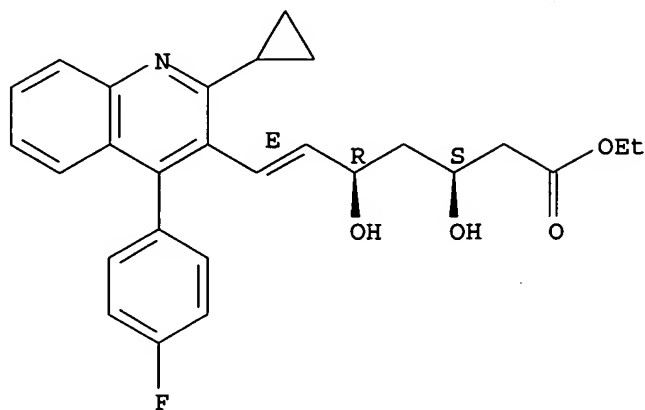
Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



● 1/2 Ca

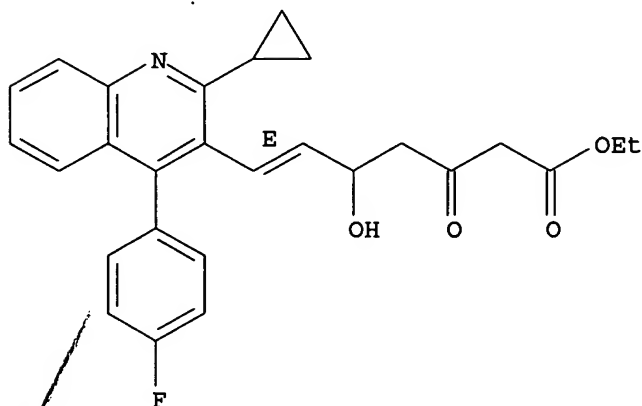
IT 147008-20-6P 148901-69-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
 RN 147008-20-6 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 148901-69-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



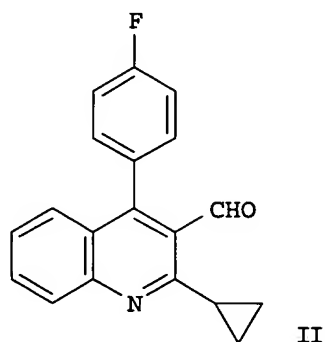
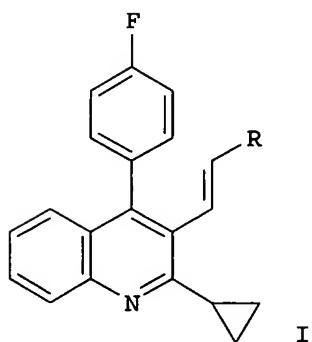
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L67 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:84775 HCAPLUS
DN 132:122527
TI Process for the preparation of quinoline derivative and intermediate therefor
IN Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Takada, Yasutaka
PA Nissan Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000005213	A1	20000203	WO 1999-JP3923	19990722 <--
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU,				

ID, IL, IN, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO,
 NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2338334	AA	20000203	CA 1999-2338334	19990722	<--
AU 9947992	A1	20000214	AU 1999-47992	19990722	<--
AU 746722	B2	20020502			
EP 1099694	A1	20010516	EP 1999-931484	19990722	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
NZ 509401	A	20020828	NZ 1999-509401	19990722	<--
CN 1107670	B	20030507	CN 1999-809003	19990722	<--
RU 2214402	C2	20031020	RU 2001-105200	19990722	<--
ZA 2001000525	A	20010801	ZA 2001-525	20010118	<--
NO 2001000357	A	20010122	NO 2001-357	20010122	<--
US 6335449	B1	20020101	US 2001-764994	20010123	<--
PRAI JP 1998-207911	A	19980723	<--		
WO 1999-JP3923	W	19990722	<--		
OS CASREACT 132:122527					
GI					



AB Claimed is a process for the preparation of 3-quinolinypropenal derivative (I; R = CHO) through quinolylacrylonitrile I (R = cyano) which can be prepared by reacting quinolinealdehyde (II) with di-Et cyanomethyl phosphonate. I (R = CHO) is useful as an intermediate for a cholesterol-lowering agent (HMG-CoA reductase inhibitor) (III.1/2Ca). Thus, 400 g 20% aqueous NaOH was added dropwise to a mixture of II 199, di-Et cyanomethylphosphonate 136, and Aliquat 336 5.5 g in 960 g PhMe at 25-35° over 0.5-1 h and stirred at the same temperature for 1 h to give, after workup and recrystn. from hexane, 88% I (R = cyano). The latter nitrile (181 g) was dissolved in 1,812 mL PhMe and cooled to -10°, followed by adding a 1.02 M solution of diisobutylaluminum (664 mmol, 650 mL) at -10° to -5° over 1 h, and the resulting mixture was stirred at the same temperature for 1 h to give, after workup and recrystn. from a mixture of cyclohexane and n-hexane, 93% I (R = CHO).

IT 147526-32-7P

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of quinolinypropenal derivative by condensation of quinolinealdehyde derivative with di-Et cyanomethylphosphonate and reduction of

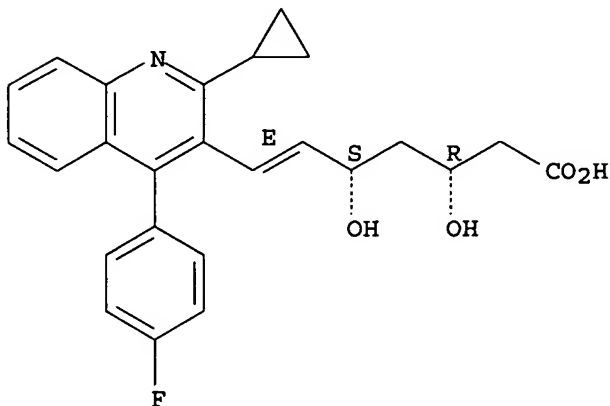
quinolylacrylonitrile derivative)

RN 147526-32-7 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



● 1/2 Ca

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:716678 HCAPLUS

DN 132:93197

TI First systematic chiral syntheses of two pairs of enantiomers with 3,5-dihydroxyheptenoic acid chain, associated with a potent synthetic statin NK-104

AU Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Kanda, Hiroyasu; Yanagihara, Kazufumi; Matsumoto, Hiroo; Ohara, Yoshio; Yazaki, Yukari; Sakoda, Ryozo

CS Central Research Institute, Nissan Chemical Industries Ltd., Chiba, 274-8507, Japan

SO Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2977-2982

CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

OS CASREACT 132:93197

AB All 4 enantiomers of the synthetic statin NK-104 were prepared The syn diol isomers (NK-104 and its enantiomer) were obtained efficiently by diastereomer resolution The anti diol isomers (3-epimer and 5-epimer) were prepared effectively by asym. aldol reaction followed by anti stereoselective reduction as key steps. Their purity detns. were effected by chiral HPLC anal.

IT 147511-70-4P 254452-87-4P 254452-91-0P
254452-95-4P

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of the enantiomers of NK-104)

RN 147511-70-4 HCAPLUS

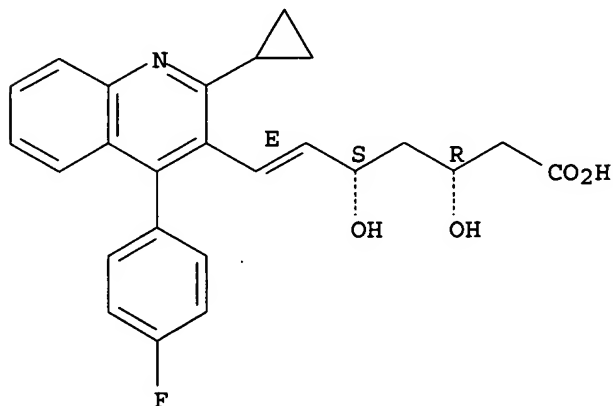
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with (α R)- α -methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1

CMF C25 H24 F N O4

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

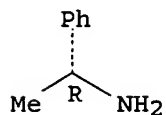


CM 2

CRN 3886-69-9

CMF C8 H11 N

Absolute stereochemistry.



RN 254452-87-4 HCAPLUS

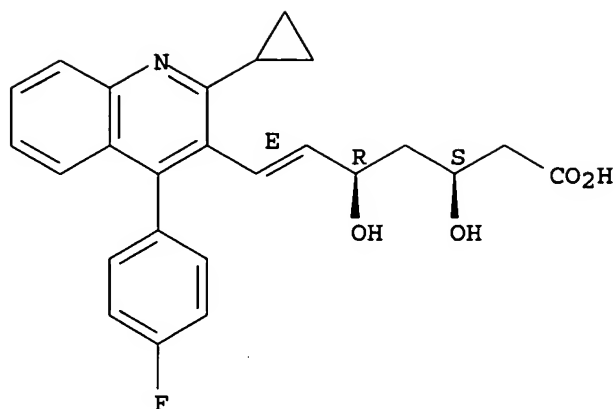
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3S,5R,6E)-, compd. with (α S)- α -methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 254452-86-3

CMF C25 H24 F N O4

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

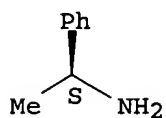


CM 2

CRN 2627-86-3

CMF C8 H11 N

Absolute stereochemistry.

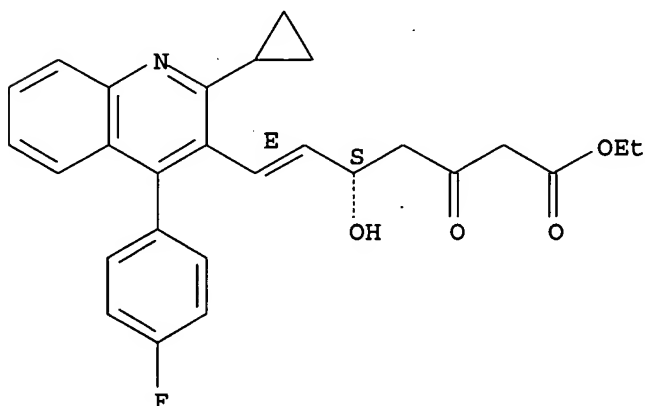


RN 254452-91-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

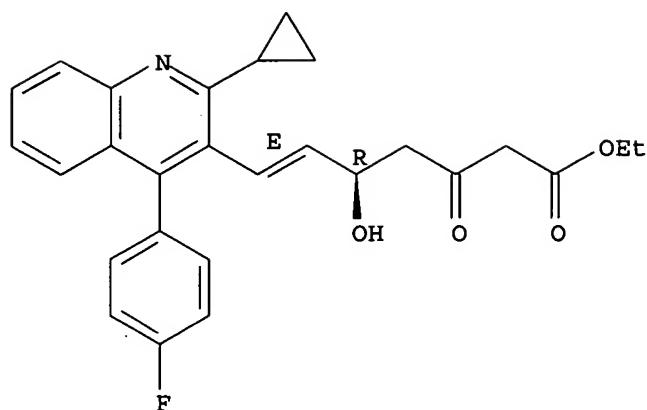


RN 254452-95-4 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (5R,6E)- (9CI) (CA INDEX NAME)

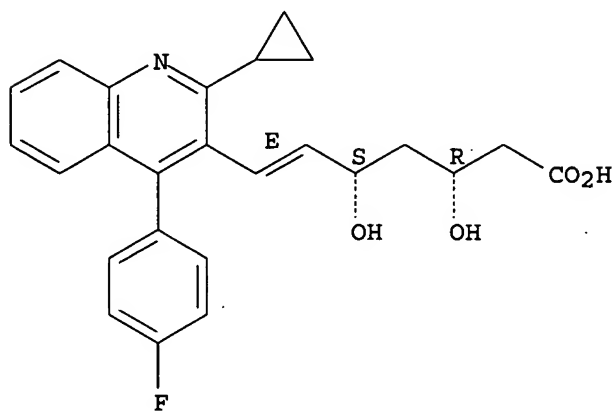
Absolute stereochemistry.

Double bond geometry as shown.



IT 147526-32-7P, NK-104 254452-88-5P, ent-NK-104
 254452-92-1P, 3-epi-NK-104 254452-96-5P, 5-epi-NK-104
 RL: PUR (Purification or recovery); SPN (Synthetic
 preparation); PREP (Preparation)
 (preparation of the enantiomers of NK-104)
 RN 147526-32-7 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
 dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

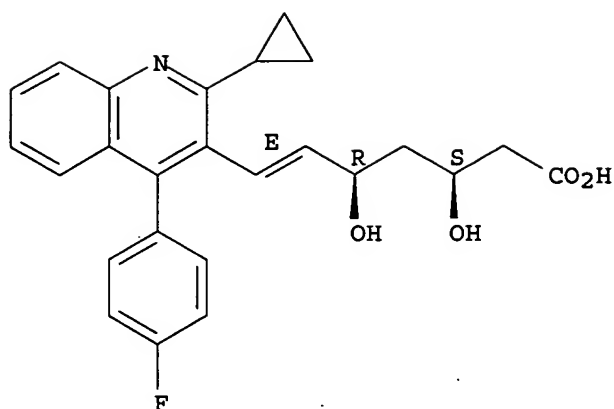
Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.



● 1/2 Ca

RN 254452-88-5 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
 dihydroxy-, calcium salt (2:1), (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as shown.

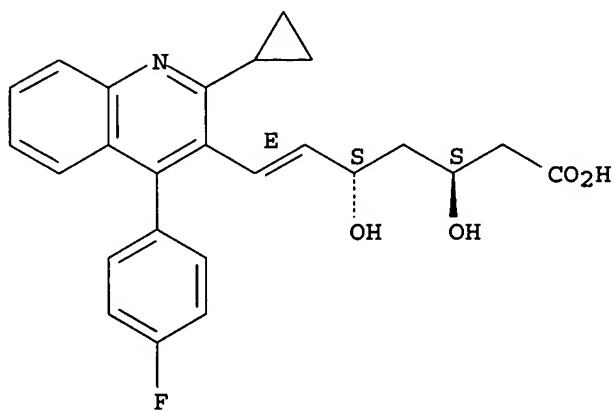


● 1/2 Ca

RN 254452-92-1 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3S,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

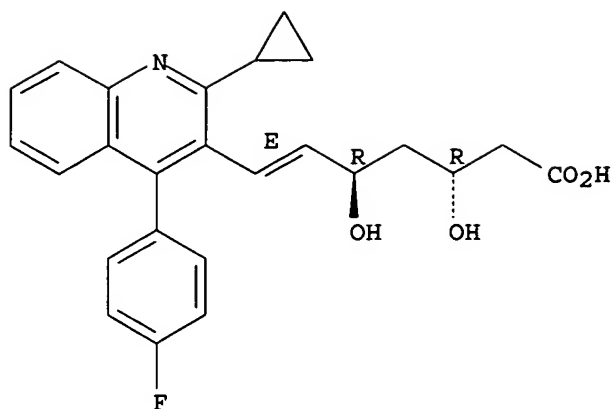


● 1/2 Ca

RN 254452-96-5 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



● 1/2 Ca

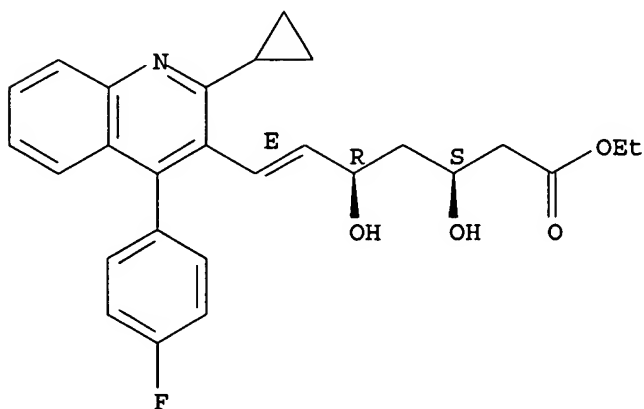
IT 147008-20-6P 148901-69-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of the enantiomers of NK-104)

RN 147008-20-6 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

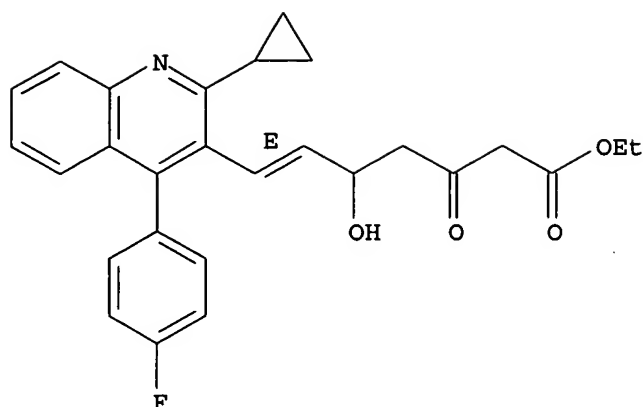
Relative stereochemistry.
Double bond geometry as shown.



RN 148901-69-3 HCAPLUS

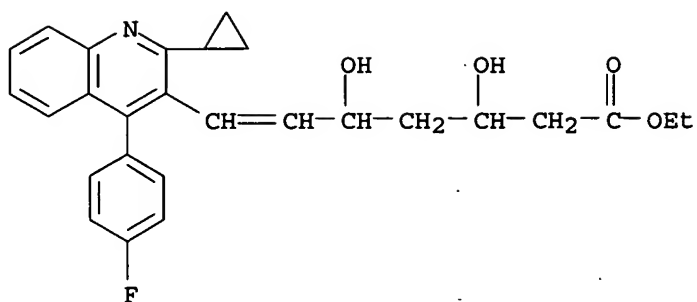
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

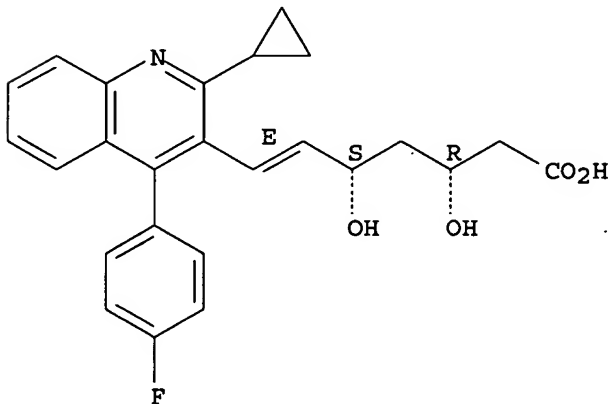
L67 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:96840 HCAPLUS
DN 130:316585
TI Chiral separation of a pharmaceutical intermediate by a simulated moving bed process
AU Nagamatsu, S.; Murazumi, K.; Makino, S.
CS Daicel Chemical Ind., Chiyoda-ku, Tokyo, 100, Japan
SO Journal of Chromatography, A (1999), 832(1 + 2), 55-65
CODEN: JCRAEY; ISSN: 0021-9673
PB Elsevier Science B.V.
DT Journal
LA English
AB The chiral separation of a pharmaceutical intermediate by a simulated moving bed (SMB) system on a pilot-scale is described. The operating conditions were chosen from results simulated by the software, help, developed by Novasep, based upon data from a single column. The productivity of the SMB system is tested by the separation of an ester of quinoline mevalonic acid at various internal flow-rates. The eluent consumption is also discussed. The step time to switch the ports to enter or withdraw solns. is one of important factors influencing the productivity.
IT 121661-13-0P, DOLE
RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chiral separation of pharmaceutical intermediate by simulated moving bed process)
RN 121661-13-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:767327 HCAPLUS
DN 130:60508
TI NK-104: hypolipidemic HMG-CoA reductase inhibitor
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (1998), 23(8), 847-859
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review, with 42 refs., of the synthesis, pharmacol., pharmacokinetics, and clin. studies of the title agents.
IT 147526-32-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MSC (Miscellaneous); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipidemic HMG-CoA reductase inhibitor)
RN 147526-32-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

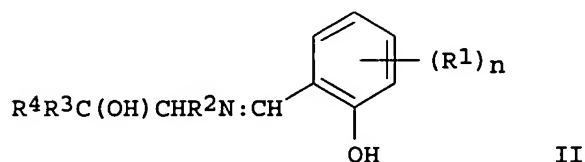
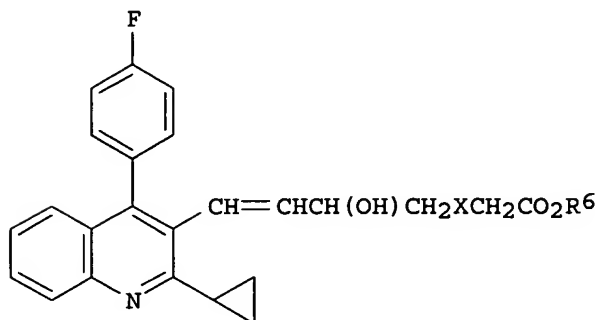
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:409680 HCAPLUS
DN 125:58345
TI Preparation of optically active quinolyldihydroxyheptenoates as
intermediates for anticholesteremics
IN Harada, Katsumasa; Matsushita, Akio; Sasaki, Hiroshi; Kawachi, Yasuhiro
PA Ube Industries, Japan; Nissan Chemical Ind Ltd
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08092217	A2	19960409	JP 1994-212958	19940906 <--
PRAI	JP 1994-212958		19940906 <--		
OS	CASREACT 125:58345; MARPAT 125:58345				
GI					



AB The title compds. I (R_6 = alkyl, Ph; X = CHO) are prepared by reaction of (E)-3-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]prop-2-en-1-al (III) with diketene in organic solvents in the presence of Ti complexes, prepared from optically active Schiff bases II (R_1 = alkyl; R_2 = H, alkyl, Ph; R_3 , R_4 = H, alkyl; $R_2 = R_3 = R_4 \neq H$; $n = 0-4$) and $Ti(OR_5)_4$ (R_5 = alkyl, Ph), followed by syn-reduction of the optically active I (X = CO). III and diketene were added to a mixture of (S)-II (R_1 = 3-CMe₃, R_2 = CHMe₂, R_3-4 = H) and $Ti(OEt)_4$ in CH_2Cl_2 and stirred at -50° for 62 h to give 72% (5S)-(E)-I (R_6 = Et, X = CO) with 78% ee, reduction of which with $NaBH_4$ and Me₂BOME in THF-MeOH at -75° for 3.5 h gave 88% (3R,5S)-(E)-I (R_6 = Et, X = CHO) (IV). IV was converted into (4R,6S)-(E)-6-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-ylethenyl]-4-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one in 89% yield and 78% ee.

IT 167073-19-0P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN

(Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

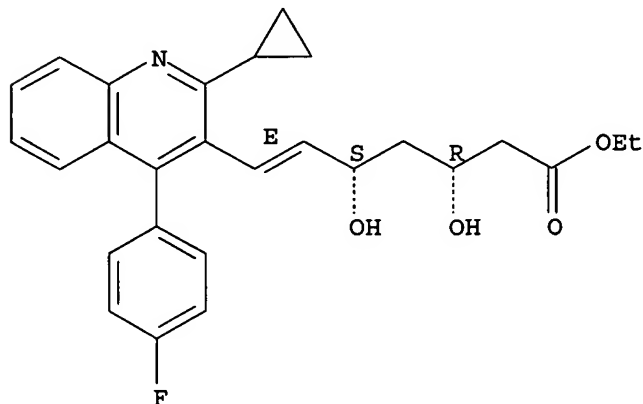
(preparation of optically active quinolyldihydroxyheptenoates from quinolylpropenal and diketene by addition with Ti complexes and reduction)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L67 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:281632 HCAPLUS

DN 124:343135

TI Preparation of quinolinaldehyde derivative as intermediate for quinoline type mevalonolactones

IN Matsumoto, Hiroo; Kanda, Hiroyasu; Obara, Yoshio; Ikeda, Hirokazu; Murakami, Tatsufumi

PA Daiseru Kagaku Kogyo Kk, Japan; Nitsusan Kagaku Kogyo Kk

SO Jpn. Kokai Tokkyo Koho, 10 pp.

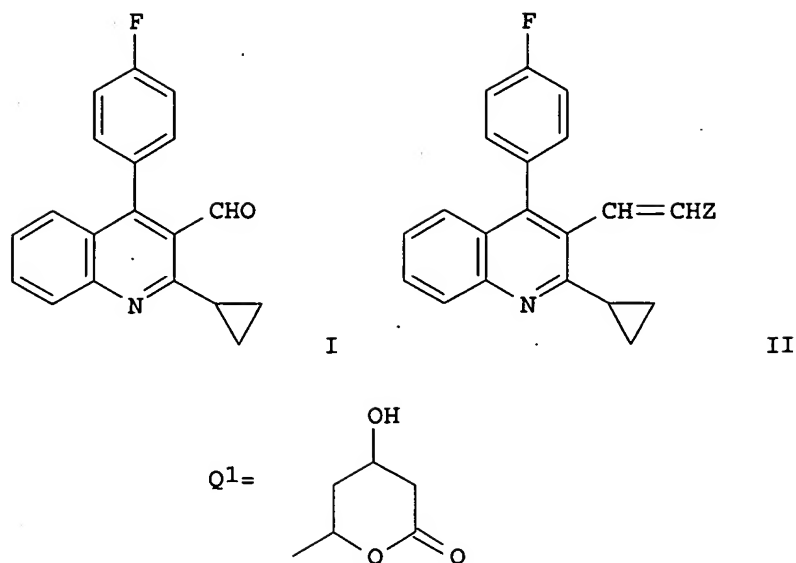
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08003138	A2	19960109	JP 1995-35587	19950223 <--
PRAI	JP 1994-28596		19940225 <--		
OS	MARPAT 124:343135				
GI					



AB The title compound I is prepared by reaction of olefin II [Z = Q1, etc.] with ozone. Thus, a mixture of ozone and oxygen was introduced into II [Z = Q1] in ethanol and methanol at -60 to -72° during 1.5 h. Dimethylsulfide was then added to the reaction mixture at -72°; and the resulting mixture was warmed to room temperature during 1 h to give, after workup, 29% I.

IT 167073-18-9P 167073-19-0P

RL: PUR (Purification or recovery); PREP (Preparation)

(preparation of quinolinaldehyde derivative as intermediate for quinoline

type

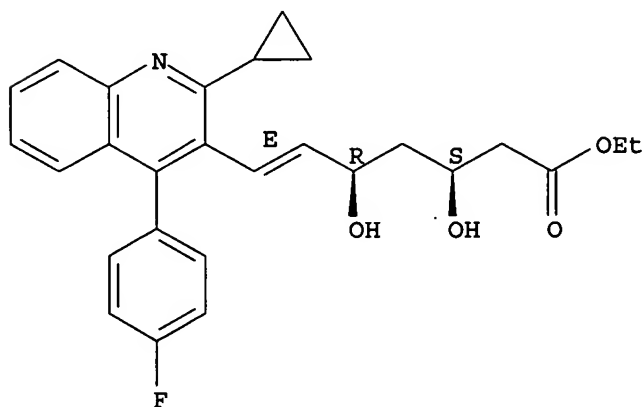
mevalonolactones)

RN 167073-18-9 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

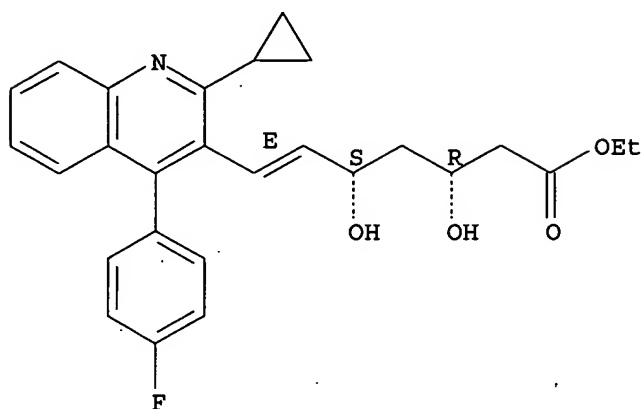
Double bond geometry as shown.



RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



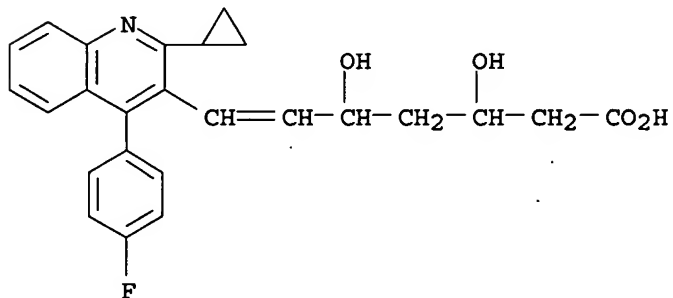
IT 121659-04-9 121661-13-0 148885-99-8
148901-69-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of quinolinaldehyde derivative as intermediate for quinoline
type mevalonolactones)

RN 121659-04-9 HCAPLUS

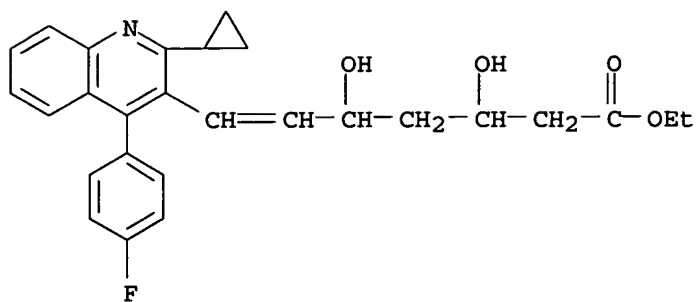
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

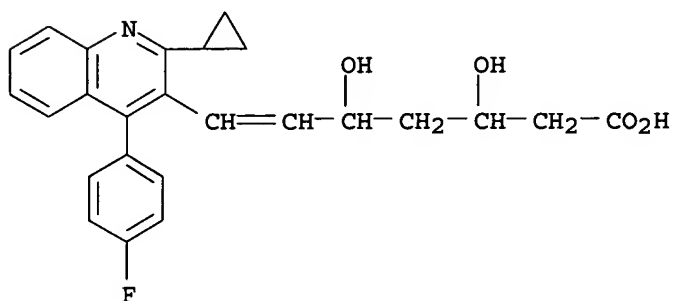
RN 121661-13-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 148885-99-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1) (9CI) (CA INDEX NAME)

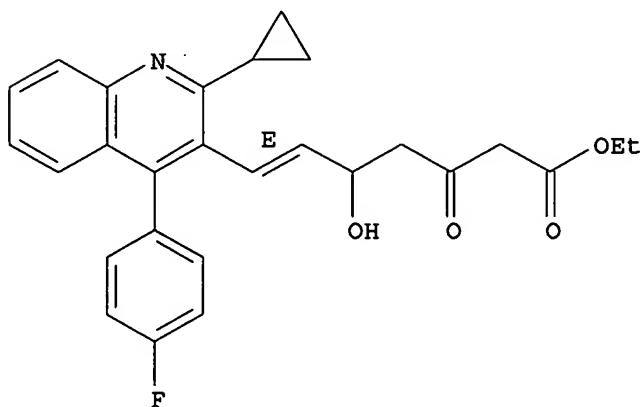


● 1/2 Ca

RN 148901-69-3 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 121659-03-8P 176593-07-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

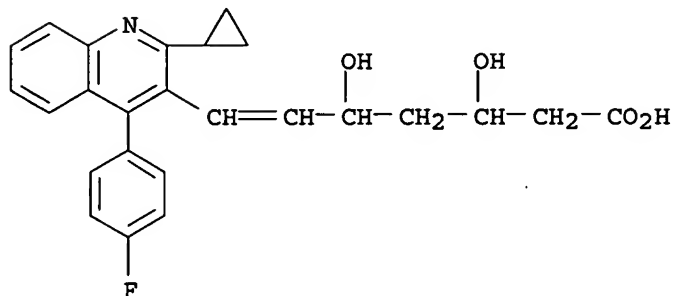
(preparation of quinolinaldehyde derivative as intermediate for quinoline

type

mevalonolactones)

RN 121659-03-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 176593-07-0 HCAPLUS

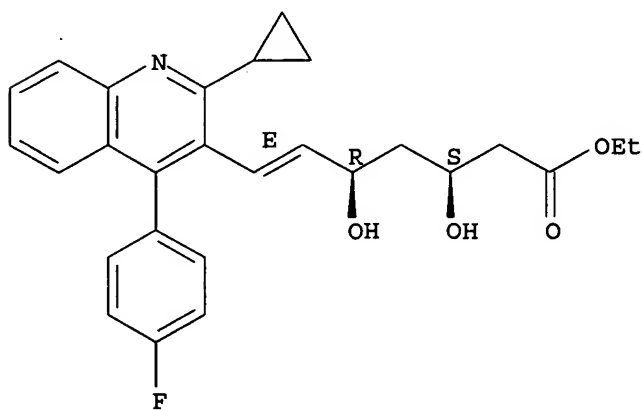
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, [R-[R*,S*-(E)]]-, compd. with (R)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 167073-18-9

CMF C27 H28 F N O4

Absolute stereochemistry.
Double bond geometry as shown.

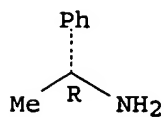


CM 2

CRN 3886-69-9

CMF C8 H11 N

Absolute stereochemistry.



L67 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:994304 HCAPLUS
 DN 124:86587
 TI Process for producing optically active aromatic mevalonolactone compounds
 IN Ikeda, Hirokazu; Murakami, Tatsushi; Matsumoto, Hiroo; Ohara, Yoshio;
 Kanda, Hiroyashu
 PA Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9523125	A1	19950831	WO 1995-JP251	19950222 <--
	W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, RO, RU, SI, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2183071	AA	19950831	CA 1995-2183071	19950222 <--
	CA 2183071	C	20011218		
	AU 9518231	A1	19950911	AU 1995-18231	19950222 <--
	AU 691582	B2	19980521		
	EP 747341	A1	19961211	EP 1995-909953	19950222 <--
	EP 747341	B1	20020522		
	R: AT, CH, DE, FR, GB, IT, LI, NL				
	HU 74486	A2	19970128	HU 1996-2291	19950222 <--
	HU 214160	B	19980128		
	AT 217859	E	20020615	AT 1995-909953	19950222 <--
	CN 1136182	B	20040128	CN 1995-191678	19950222 <--
	US 5939552	A	19990817	US 1996-700396	19960822 <--
PRAI	JP 1994-28594	A	19940225 <--		
	WO 1995-JP251	W	19950222 <--		

AB A mevalonolactone compound is produced by batchwise chromatog. or pseudo-moving bed method both using a column filled with a packing material for optical resolution comprising a polysaccharide derivative The pseudo-moving bed method comprises jointing endlessly a number of columns to form a circulating flow path wherein a fluid is forcibly circulated in one direction, providing alternately along the direction of flow of the circulated fluid inlets for feeding the fluid into the column and outlets for drawing the fluid out of the column, moving intermittently the positions of the inlets and the outlets in the direction of flow of the circulated fluid, feeding a solution containing a racemate of a mevalonolactone compound and an eluent into a circulating path through the inlets, and drawing out simultaneously a solution enriched with nonadsorbates and a solution enriched with adsorbates through the outlets.

IT 172336-33-3

RL: ANT (Analyte); ANST (Analytical study)

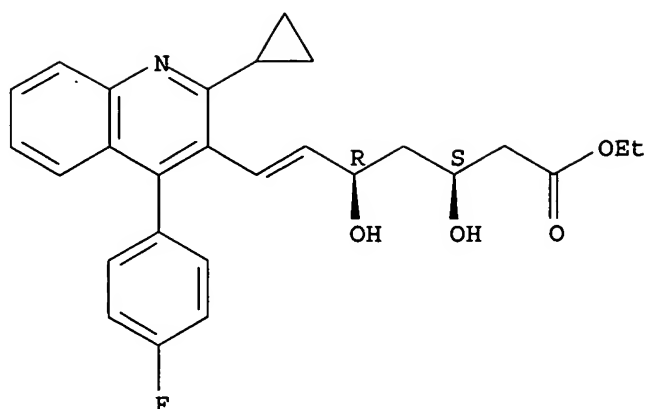
(process for producing optically active mevalonolactone compound)

RN 172336-33-3 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry unknown.



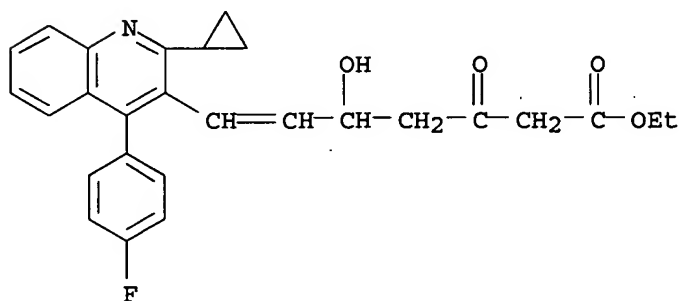
IT 121660-87-5P 172336-32-2P

RL: PUR (Purification or recovery); PREP (Preparation)

(process for producing optically active mevalonolactone compound)

RN 121660-87-5 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)

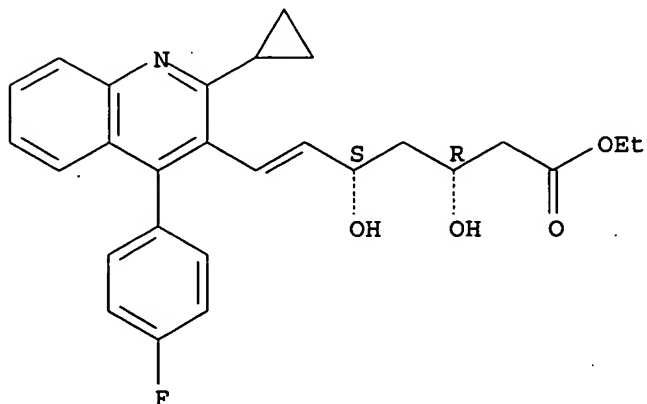


RN 172336-32-2 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry unknown.



L67 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:750499 HCAPLUS

DN 123:168993

TI Optically active β -aminoalkoxyborane complex as asymmetric reducing agent

IN Kashiwara, Hiroshi; Suzuki, Mikio; Ohara, Yoshio

PA Nissan Chemical Industries Ltd., Japan

SO PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9417079	A1	19940804	WO 1994-JP56	19940117 <--
	W: AU, CA, CN, CZ, FI, HU, KR, NO, NZ, RO, RU, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	JP 06329679	A2	19941129	JP 1993-332498	19931227 <--
	TW 383309	B	20000301	TW 1994-83100279	19940114 <--
	AU 9458431	A1	19940815	AU 1994-58431	19940117 <--
	AU 678427	B2	19970529		
	EP 680484	A1	19951108	EP 1994-904332	19940117 <--
	EP 680484	B1	19980819		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1116850	A	19960214	CN 1994-190966	19940117 <--
	CN 1047173	B	19991208		
	HU 72018	A2	19960328	HU 1995-2184	19940117 <--
	HU 217182	B	19991228		
	AT 169921	E	19980915	AT 1994-904332	19940117 <--
	RU 2126412	C1	19990220	RU 1995-115845	19940117 <--
	ZA 9400383	A	19940907	ZA 1994-383	19940119 <--
	IL 108387	A1	20000629	IL 1994-108387	19940120 <--
	NO 9502870	A	19950919	NO 1995-2870	19950719 <--
	US 5663348	A	19970902	US 1995-481505	19950719 <--
	US 5767277	A	19980616	US 1997-779621	19970107 <--
	US 5739347	A	19980414	US 1997-848173	19970429 <--
	US 5786485	A	19980728	US 1997-848172	19970429 <--
	US 5808098	A	19980915	US 1997-848169	19970429 <--
	US 5852221	A	19981222	US 1997-848174	19970429 <--
	NO 9805016	A	19950919	NO 1998-5016	19981028 <--
	CN 1234392	A	19991110	CN 1999-105088	19990409 <--
PRAI	JP 1993-7827	A	19930120		<--
	JP 1993-66825	A	19930325		<--
	WO 1994-JP56	W	19940117		<--
	US 1995-481505	A3	19950719		<--
OS	MARPAT 123:168993				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Optically active β -aminoalkoxyborane complexes are disclosed, specifically I [R1 = C1-C8 alkyl, C3-C7 cycloalkyl, C7-C11 aralkyl or C6-C10 aryl; R2 = H, C1-C8 alkyl, C3-C7 cycloalkyl or C7-C11 aralkyl; or R1R2 = (CH2)_n wherein n = 3 or 4; Ar = naphthyl, anthryl or phenanthryl, which may be substituted by 1-3 substituents selected from halo, nitro, C1-C6 alkyl, C3-C7 cycloalkyl, C2-C6 alkenyl or alkynyl, C7-C11 aralkyl, C6-C10 aryl, C1-C6 alkoxy, and styrene polymer substituents]. The complexes are useful for reducing carbonyl compds. to optically active alcs., and especially for reducing 1,3-dicarbonyl compds. to optically active

1,3-syn-diols. For example, reduction of proline Et ester with LiAlH_4 to give (S)-prolinol, cyclocondensation of this with β -naphthaldehyde to give an oxazolidine derivative (quant.), reduction of this with NaBH_4 to give an amino

alc. (quant.), and reaction of the latter with $\text{BH}_3\cdot\text{THF}$ (quant.), gave the (S)-isomeric complex II. Reduction of diketo ester III using II and Et_2BOMe in THF at 20° gave the (3S,5R)-syn-diol IV in 53% yield and 100% enantiomeric excess (ee). In contrast, several similar known borane complexes gave 28-78% yield but only 6-23% ee.

IT 167073-18-9P, (3S,5R,E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate

167073-19-0P, (3R,5S,E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

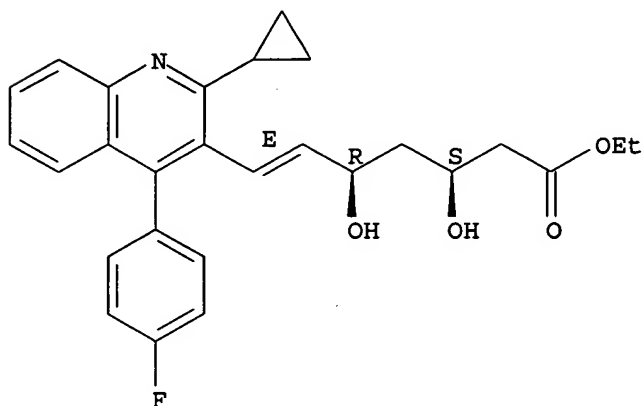
(reduction product; preparation of optically active β -aminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)

RN 167073-18-9 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

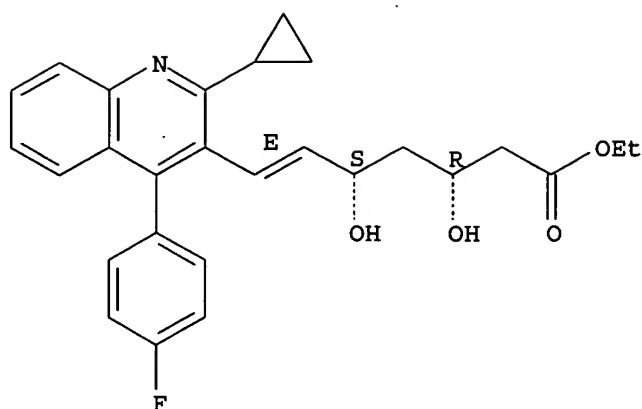


RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

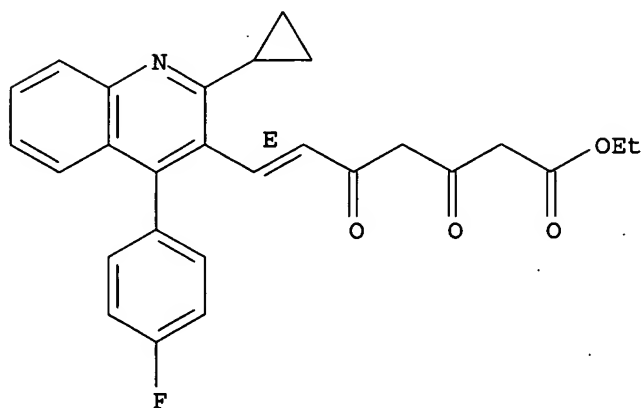
Absolute stereochemistry.

Double bond geometry as shown.

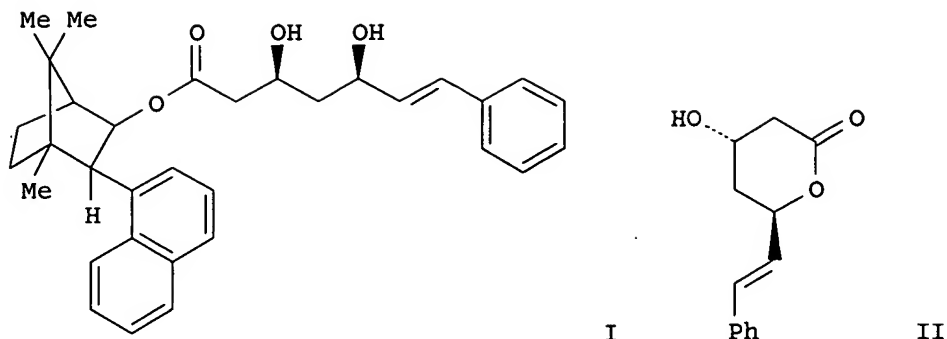


IT 166803-31-2P, (E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dioxo-6-heptenoate
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (reduction substrate; preparation of optically active β -aminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)
 RN 166803-31-2 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L67 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:330180 HCAPLUS
 DN 123:285697
 TI Stereoselective reduction of β,δ -diketo esters. A novel strategy for the synthesis of artificial HMG-CoA reductase inhibitors
 AU Hiyama, Tamejiro; Reddy, Guntoori Bhaskar; Minami, Tatsuya; Hanamoto, Takeshi
 CS Sagami Chem. Research Center, Kanagawa, 229, Japan
 SO Bulletin of the Chemical Society of Japan (1995), 68(1), 350-63
 CODEN: BCSJA8; ISSN: 0009-2673
 PB Nippon Kagakkai
 DT Journal
 LA English
 GI



AB Condensation of N-methoxy-N-Me amides with acetoacetate dianions gave β,δ -diketo esters, which were selectively reduced with Et₂BOMe-NaBH₄ in THF/MeOH to give syn- β,δ -dihydroxy esters in one step. Similarly, the β,δ -diketo esters of the Taber's chiral alc. or its enantiomer resp. were reduced to give syn- β,δ -dihydroxy esters of moderate enantiomeric excess. Higher diastereoselective and enantioselectivity were achieved by reduction of the β,δ -diketo esters of Taber's chiral alc. or its enantiomer successively with diisobutylalane and with Et₂BOMe-NaBH₄. The resulting syn-diol esters were hydrolyzed and lactonized to give various types of β -hydroxy- δ -lactones commonly found in artificial HMG-CoA reductase inhibitors; pharmacol. test data were not shown. The precursor I was converted to the example compound [4S-[4 α ,6 β (E)]]-tetrahydro-4-hydroxy-6-(2-phenylethenyl)-2H-pyran-2-one (II).

IT 141750-57-4P 141750-58-5P 141750-61-0P

155899-28-8P

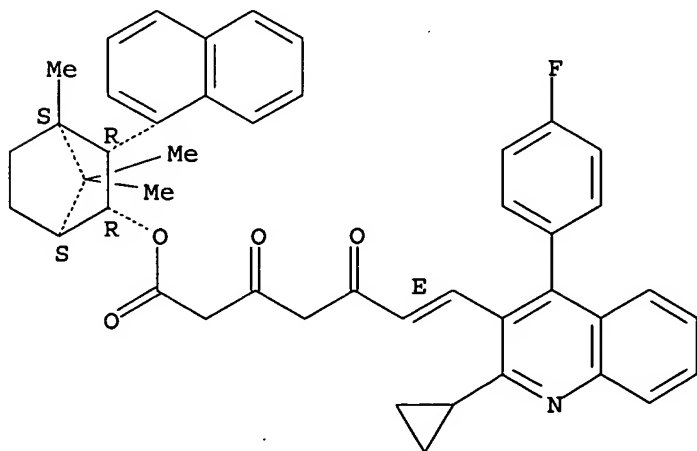
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of β -hydroxy- δ -lactones as HMG-CoA reductase inhibitors)

RN 141750-57-4 HCAPLUS

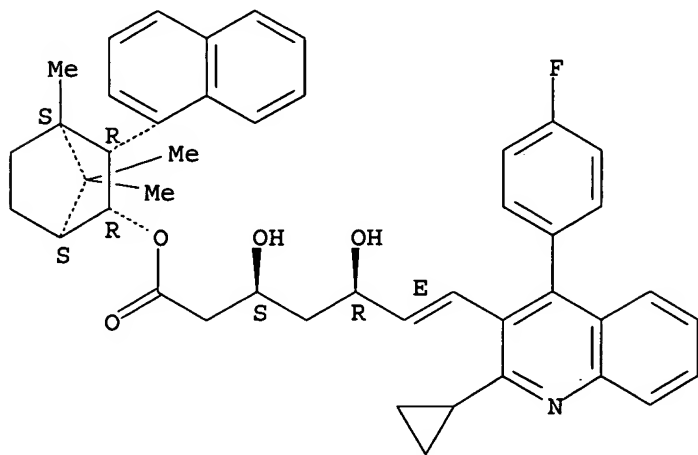
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



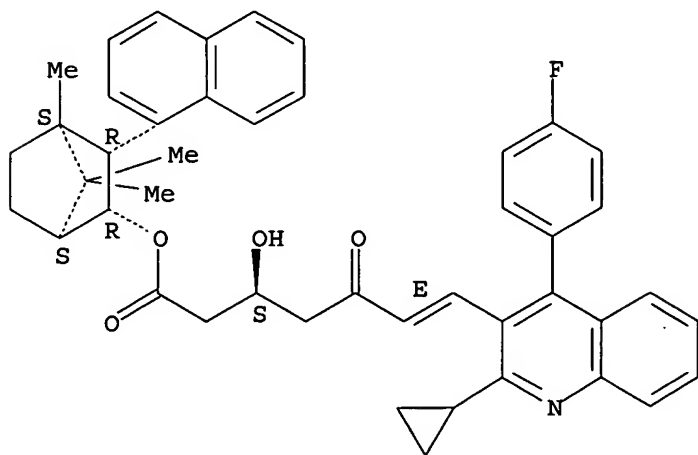
RN 141750-58-5 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (3R*,5S*,6E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



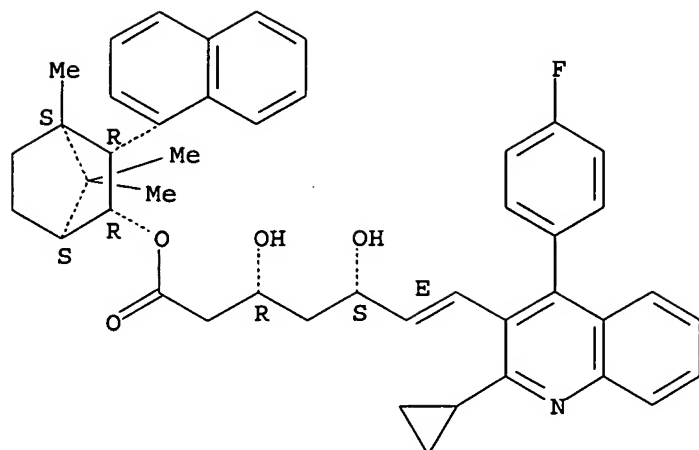
RN 141750-61-0 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (3R*,6E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



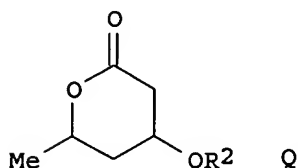
RN 155899-28-8 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (3S*,5R*,6E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L67 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:304888 HCAPLUS
 DN 122:105264
 TI preparation of 6-heptynoic and heptenoic acid compounds as intermediates
 for HMG-CoA reductase inhibitors
 IN Hiyama, Tamejiro; Minami, Tatsuya; Takahashi, Kyoko; Miyachi, Nobuhide;
 Ohara, Yoshio
 PA Nissan Chemical Industries Ltd., Japan; Sagami Chemical Research Center
 SO PCT Int. Appl., 86 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9406746	A1	19940331	WO 1993-JP1349	19930921 <--
	W: AU, CA, CZ, FI, HU, KR, NO, NZ, RO, RU, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9306732	A	19940411	ZA 1993-6732	19930913 <--
	JP 06316584	A2	19941115	JP 1993-233018	19930920 <--
	AU 9349845	A1	19940412	AU 1993-49845	19930921 <--
	CN 1088204	A	19940622	CN 1993-117822	19930921 <--
PRAI	JP 1992-251413	A	19920921	<--	
	JP 1993-9489	A	19930122	<--	
	JP 1993-47878	A	19930309	<--	
	WO 1993-JP1349	W	19930921	<--	
OS	CASREACT 122:105264; MARPAT 122:105264				
GI					



AB Title compds. R6-C.tplbond.C-Z [I; Z = A-CH2-B-CH2-CO-OR1, Q; A = CO, CHOR1; R1 = H, protecting group; B = CO, CHOR2; R2 = H, protecting group; or R1R2 = part of a ring; R3 = H, C1-8 alkyl, aralkyl, aryl, silyl, etc.; R6 = H, protecting group], useful as intermediates for HMG-CoA reductase inhibitors, are prepared The use of the invention compds. and process

enables an efficient production of a 7-substituted-3,5-dihydroxy carboxylic acid compound useful as an HMG-CoA reductase inhibitor. E.g., I [R6 = trimethylsilyl (TMS), Z = CH(OH)-CH₂-CH(OH)-CH₂-CO-OEt] was prepared via condensation of TMS-C.tplbond.C-CHO (preparation given) with Et acetoacetate.

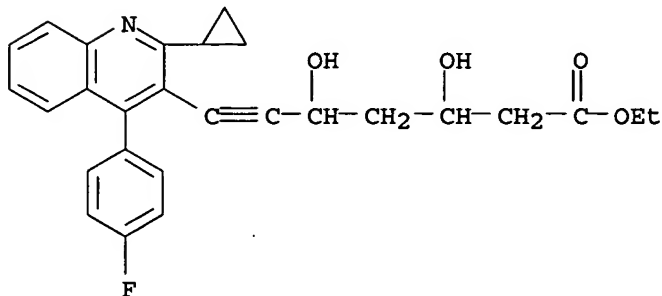
IT 156782-70-6P 160375-26-8P 160375-27-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for HMG-CoA reductase inhibitors)

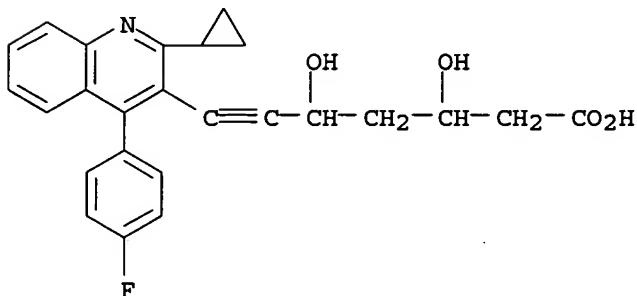
RN 156782-70-6 HCAPLUS

CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



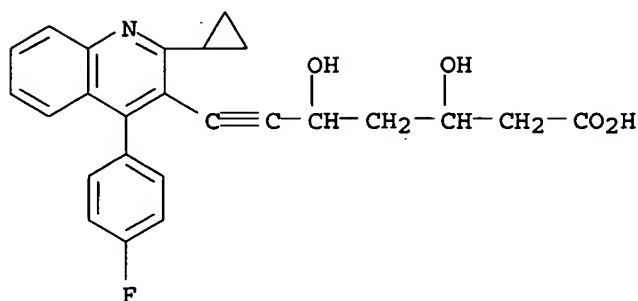
RN 160375-26-8 HCAPLUS

CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 160375-27-9 HCAPLUS

CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1) (9CI) (CA INDEX NAME)



● 1/2 Ca

L67 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:508553 HCAPLUS
 DN 121:108553
 TI Preparation of 7-(4-phenyl-3-quinoliny)-3,5-dihydroxyhept-6-ynoic acid derivatives as 3-hydroxy-3-methylglutaric acid coenzyme A (HMG-CoA) reductase inhibitors
 IN Obara, Yoshio; Myaji, Nobuhide; Kitahara, Maki
 PA Nissan Chemical Ind Ltd, Japan
 SO Jpn. Kokai Tokkyo Koho, 39 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06116239	A2	19940426	JP 1992-266264	19921005 <--
PRAI	JP 1992-266264		19921005		
OS	MARPAT 121:108553				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; X = 5- to 6-membered heteroaryl or (un)substituted Ph ring; R1, R2 = H, C1-8 alkyl, C3-7 cycloalkyl, C1-3 alkoxy, BuO, iso-, sec-, or tert-BuO, R20R21N (wherein R20, R21 = H, C1-3 alkyl), CF3, CF3O, CF2H, F, Cl, Br, Ph, PhO, PhCH2O, OH, Me3SiO, Me3CPh2SiO, HOCH2, O(CH2)1OR22 (wherein R22 = H, C1-3 alkyl; 1 = 1,2,3); adjacent R1 and R2 form CH:CHCH:CH or OCH2O; R3 = H, C1-8 alkyl, C2-6 alkenyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, (un)substituted Ph, C1-3 alkyl substituted by Ph and 0-2 C1-3 alkyl; Z = Z1CH2WCH2CO2R12, Q, Q1, Q2; Z1 = CO, C(OR13)2, CHOH; W = CO, C(OR13)2, CR11OH; R11 = H, C1-3 alkyl; R12 = H, alkyl of chemical or physiol. hydrolyzable alkyl ester, NHR23R24R25 (wherein R23, R24, R25 = H, C1-4 alkyl), Na, K, 1/2Ca; R13 = primary or secondary C1-6 alkyl or 2R13 = CH2CH2 or (CH2)3; R15, R16 = H, C1-3 alkyl or R15R16 = CH2CH2 or (CH2)3], useful for the treatment of hypercholesteremia, hyperlipoproteinemia, and atheromatous arteriosclerosis, are prepared Thus, 3-cyclopropyl-4-(4'-fluorophenyl)-3-iodoquinoline 60, CuI 8, Pd(PPh3)2Cl2 13, and 0.8 mL Et2NH were added to 42 mg Et 3,5-O-isopropylidene-3,5-dihydroxy-6-heptynoate followed by stirring at room temperature for 4 h to give 36% phenylquinoline derivative (II; RR = CMe2; M = Et) which was treated with p-MeC6H4SO3H in aqueous THF to give II (R = H; M = Et) (III). The latter

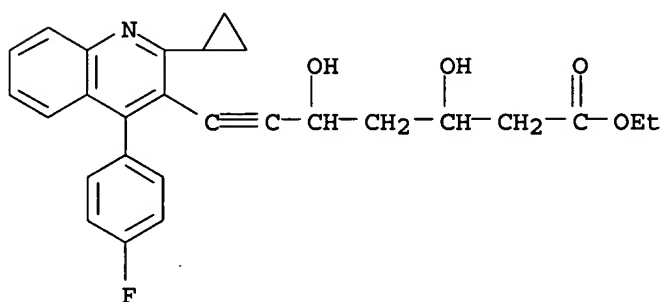
ester was saponified by aqueous 1 N NaOH and EtOH followed by acidification with aqueous 1 N HCl and conversion of the resulting free carboxylic acid to Ca salt to give $\text{II} \cdot 1/2\text{Ca}$ ($R = M = H$) (IV). III and IV at 100 nM in vitro inhibited 43.8 and 54.6%, resp., the cholesterol synthesis from AcOH in rat liver microsome prepn, in which HMG-CoA reductase is the rate determining enzyme. Tablet, capsule, ointment, suppository, injection, and granule formulations containing III were described.

IT 156782-70-6P 156782-72-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as HMG-CoA reductase inhibitor)

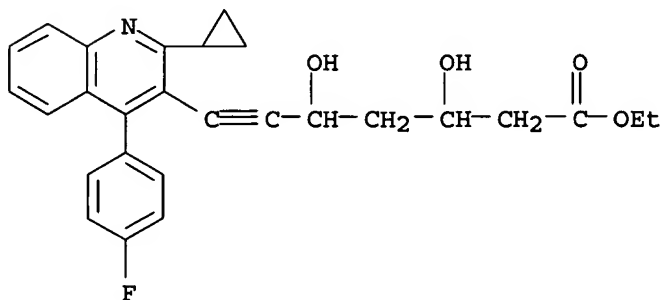
RN 156782-70-6 HCAPLUS

CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 156782-72-8 HCAPLUS

CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, calcium salt (2:1) (9CI) (CA INDEX NAME)



● 1/2 Ca

L67 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:435341 HCAPLUS

DN 121:35341

TI Preparation of optically active β,δ -diketo acid derivatives

IN Hyama, Tamejiro; Minami, Tatsuya; Guntoori, Basukaaru Redei; Sakota, Ryozo; Arai, Kazutaka; Obara, Yoshio; Suzuki, Mikio

PA Sagami Chem Res, Japan; Nissan Chemical Ind Ltd

SO Jpn. Kokai Tokkyo Koho, 20 pp.

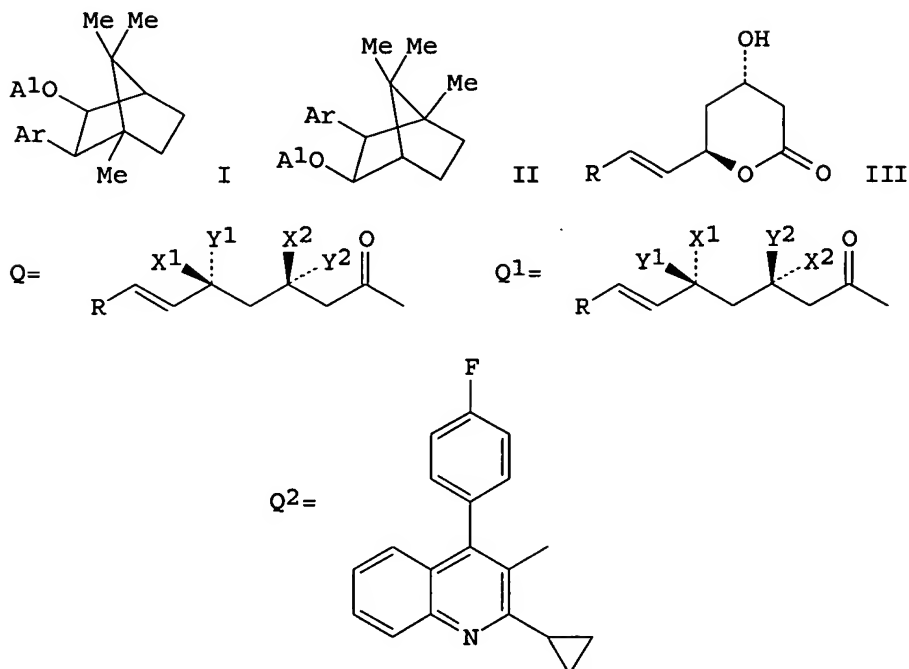
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06025092	A2	19940201	JP 1991-291586	19911107 <--
PRAI	JP 1991-291586		19911107 <--		
OS	CASREACT 121:35341; MARPAT 121:35341				
GI					



AB 2-Exo-(hetero)arylheptenoyloxy-3-exo-aryl-4,7,7-trimethylbicyclo[2.2.1]heptane derivs. [I; A1 = (un)substituted (hetero)aryl or vinyl; Ar = condensed aryl; X1, Y1 = H, OH or X1Y1 = O; X2, Y2 = H, OH or X2Y2 = O] and enantiomers thereof are prepared by treatment of acetoacetate derivs. I (A1 = MeCOCH2CO) with a base to generate a dianion followed by condensation with N-alkoxyamides trans-RCH:CHCONR1OR2 (Ar = same as above; R1, R2 = C1-4 linear or branched alkyl) and stereoselective reduction of the resulting β,δ -diketo acid derivs. I (A1 = trans-RCH:CHCOCH2COCH2CO). These derivs. I are useful as intermediates for 7-(R-substituted)-(E,3R,5S)-3,5-dihydroxy-6-heptenoic acid 1,5-lactones, hypocholesteremics, having hydroxymethylglutaryl-CoA (HMG-CoA) reductase-inhibitory activity. Thus, acetoacetate ester II (Ar = 2-naphthyl, A1 = MeCOCH2CO) was treated with NaH in THF at 0° followed by addition of BuLi/hexane at 0° and cooling to -78° and a solution of a N-methoxy-N-methylamide trans-RCH:CHCONMeOMe (R = Q2) (preparation given) in THF was added to give, after stirring at -78° to 0° for 3 h, 48% quinolyldioxoheptenoic acid derivative I (A1 = trans-RCH:CHCOCH2COCH2CO, R = Q2, Ar = 2-naphthyl). The latter compound was reduced by NaBH4 in the presence of Et2BOMe in THF/MeOH at -78° to room temperature to give quinolyldihydroxyheptenoic acid ester 90% (A1 = Q1, R = Q2, X1 = X2 = OH, Y1 = Y2 = H, Ar = 2-naphthyl) which was saponified with aqueous NaOH in MeOH and lactonized by refluxing in toluene to give lactone III (R = Q2) of 58% e.e. as a 77:23 mixture of trans/cis isomers.

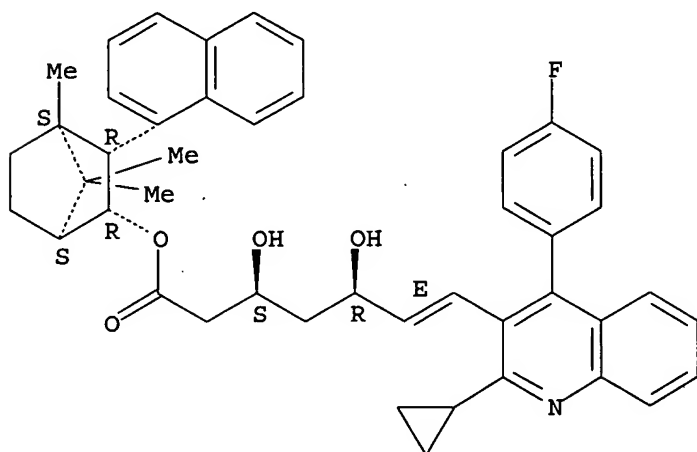
IT 141750-58-5P 155899-28-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and saponification-lactonization of)

RN 141750-58-5 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl
ester, [1S-[1 α ,2 α (3R*,5S*,6E),3 α ,4 α]]- (9CI) (CA
INDEX NAME)

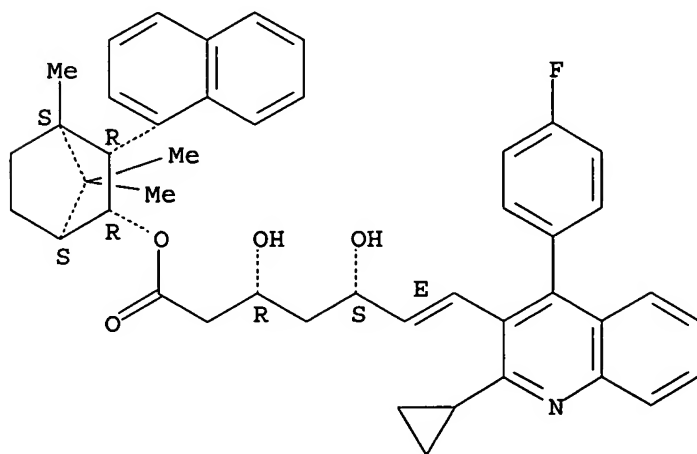
Absolute stereochemistry.
Double bond geometry as shown.



RN 155899-28-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl
ester, [1S-[1 α ,2 α (3S*,5R*,6E),3 α ,4 α]]- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



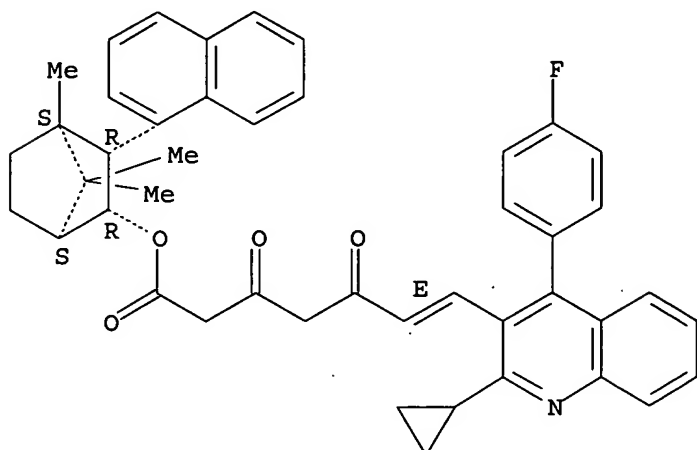
IT 141750-57-4P 141750-61-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and stereoselective reduction of)

RN 141750-57-4 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

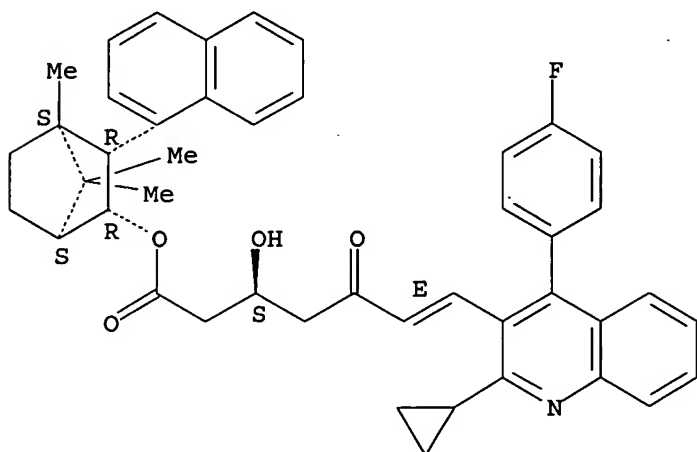
Absolute stereochemistry.
Double bond geometry as shown.



RN 141750-61-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (3R*,6E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L67 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:517112 HCAPLUS

DN 119:117112

TI Preparation of (heterocyclylvinyl)mevalonic lactone analogs as antiatherosclerotics

IN Saito, Yasushi; Kitahara, Masaki; Sakashita, Mitsuaki; Toyoda, Kyomi; Shibazaki, Toshie

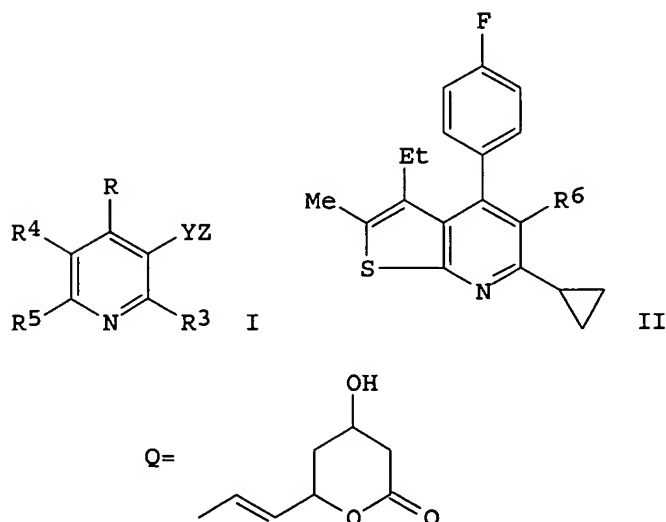
PA Nissan Chemical Industries, Ltd., Japan; Kowa Co., Ltd.

SO Eur. Pat. Appl., 64 pp.

CODEN: EPXXDW

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 535548	A1	19930407	EP 1992-116417	19920924 <--
	EP 535548	B1	20011121		
	R: AT, BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
	JP 06329540	A2	19941129	JP 1991-257870	19911004 <--
	JP 3130342	B2	20010131		
	AT 209035	E	20011215	AT 1992-116417	19920924 <--
	AU 9226012	A1	19930408	AU 1992-26012	19920928 <--
	AU 652669	B2	19940901		
	NZ 244555	A	20000623	NZ 1992-244555	19920930 <--
	US 6162798	A	20001219	US 1992-953716	19920930 <--
	NO 9203858	A	19930405	NO 1992-3858	19921002 <--
	CA 2079706	AA	19930415	CA 1992-2079706	19921002 <--
	HU 62794	A2	19930628	HU 1992-3138	19921002 <--
	HU 214624	B	19980428		
	CZ 281786	B6	19970115	CZ 1992-3027	19921002 <--
	RU 2114620	C1	19980710	RU 1992-5052949	19921002 <--
	SK 279277	B6	19980909	SK 1992-3027	19921002 <--
PRAI	JP 1991-257870	A	19911004 <--		
OS	MARPAT 119:117112				
GI					



AB Title compds. [I; R = substituted-Ph; R₃ = H, (cyclo)alkyl, (cyclo)alkenyl, (substituted)Ph, etc.; R₄R₅ = atoms to complete a fused benzene or 5- or 6-membered heteroaryl ring; Y = CH₂, CH₂CH₂, CH:CH, etc.; Z = 4-hydroxy-2-oxo- or 2,4-dioxo-6-tetrahydropyranyl, QCH₂WCH₂CO₂R₁₂, etc.; Q = CO, CH(OH), etc.; R₁₂ = H, ammonium, physiol. labile ester residue, etc.; W = CO, CH(OH), etc.], inhibitors of atherosclerotic intimal thickening, were prepared. Thus, thienopyridinecarboxyaldehyde II (R₆ = CHO) was condensed with Bu₃SnC(OEt):CH₂ and the product hydrolyzed to give II [R₆ = (E)-CH:CHCHO] which was condensed with MeCOCH₂CO₂Et to give, in 3 addnl. steps, II (R₆ = oxopyranylvinyl group Q). The latter gave 100% inhibition of smooth muscle cell proliferation at 10⁻⁶ M (intimal) and 10⁻⁵ M (medial) in vitro.

IT 121661-13-0P 148901-69-3P

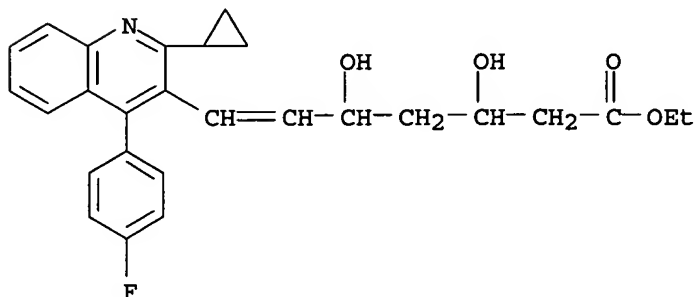
RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of antiatherosclerotic)

RN 121661-13-0 HCAPLUS

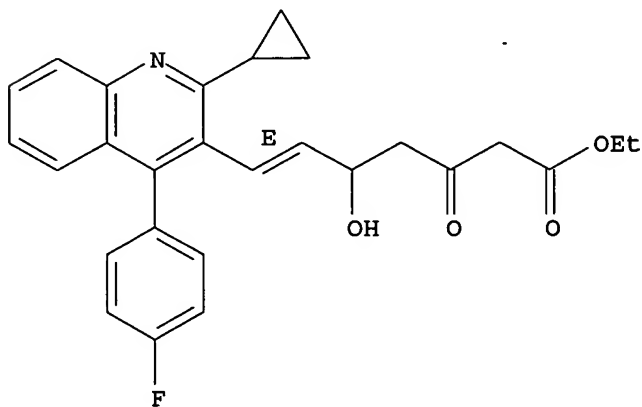
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 148901-69-3 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



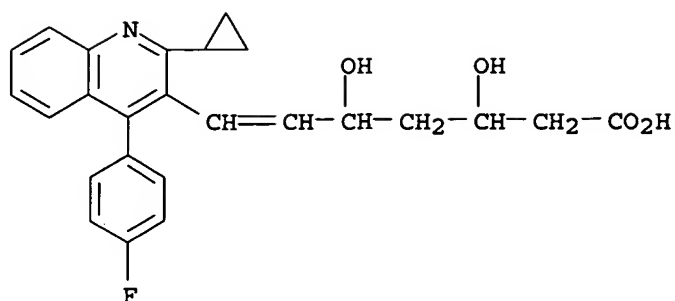
IT 121659-03-8P 121659-04-9P 148885-99-8P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as antiatherosclerotic)

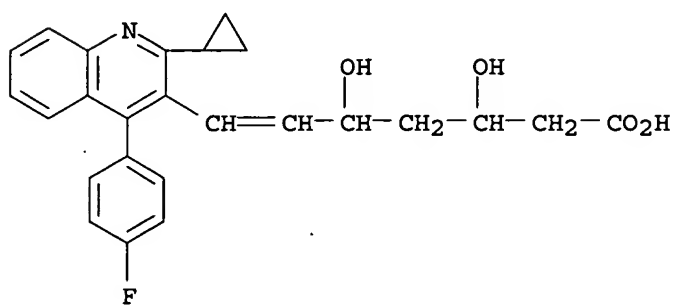
RN 121659-03-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 121659-04-9 HCAPLUS

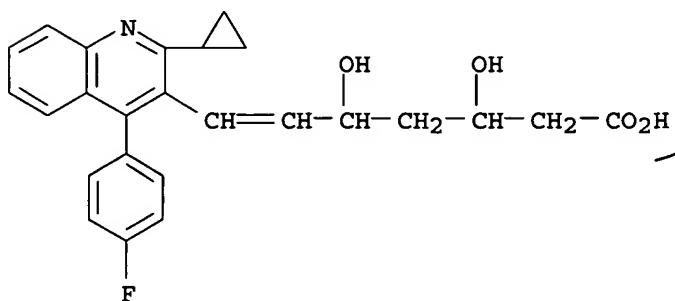
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 148885-99-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1) (9CI) (CA INDEX NAME)



● 1/2 Ca

L67 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:233897 HCAPLUS

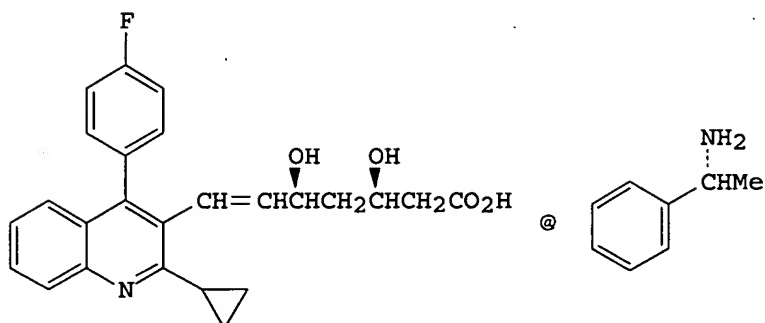
DN 118:233897

TI Preparation of diastereomer salt of optically active quinolinemevalonic

acid
 IN Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi;
 Miyachi, Nobuhide
 PA Nissan Chemical Industries, Ltd., Japan
 SO Eur. Pat. Appl., 15 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 520406	A1	19921230	EP 1992-110636	19920624 <--
	EP 520406	B1	19980902		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	JP 05148237	A2	19930615	JP 1992-127277	19920520 <--
	JP 3528186	B2	20040517		
	CA 2072162	AA	19921225	CA 1992-2072162	19920623 <--
	CA 2072162	C	20021119		
	US 5284953	A	19940208	US 1992-902863	19920623 <--
	EP 742209	A2	19961113	EP 1996-107815	19920624 <--
	EP 742209	A3	19970514		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	AT 170513	E	19980915	AT 1992-110636	19920624 <--
	ES 2120973	T3	19981116	ES 1992-110636	19920624 <--
	US 5473075	A	19951205	US 1993-123117	19930920 <--
	US 5514804	A	19960507	US 1995-450383	19950525 <--
PRAI	JP 1991-151810	A	19910624 <--		
	JP 1992-127277	A	19920520 <--		
	US 1992-902863	A3	19920623 <--		
	EP 1992-110636	A3	19920624 <--		
	US 1993-123117	A3	19930920 <--		

GI



I

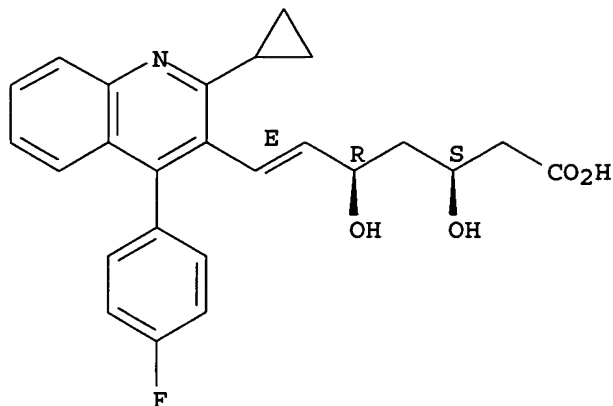
AB A diastereomer salt of the title compound (I) which is an intermediate for preparation of optically active quinolinemevalonic acid derivs. with known. biol. activity is prepared by resolution of its racemic parent. Et (+)-(E)-3,5-dihydroxy-7-[4-(4-fluorophenyl)-2-cyclopropyl-3-quinolinyl]-6-heptenoate in EtOH was added to 1N NaOH to give the free acid. To the CH_2Cl_2 solution of the free acid 1 equiv of D-(+)-PhCH(NH₂)Me was added to give the (E)-(3R,5S)-I.

IT 147008-21-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and resolution of)

RN 147008-21-7 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-

dihydroxy-, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



IT 147511-70-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ring closure of)

RN 147511-70-4 HCAPLUS

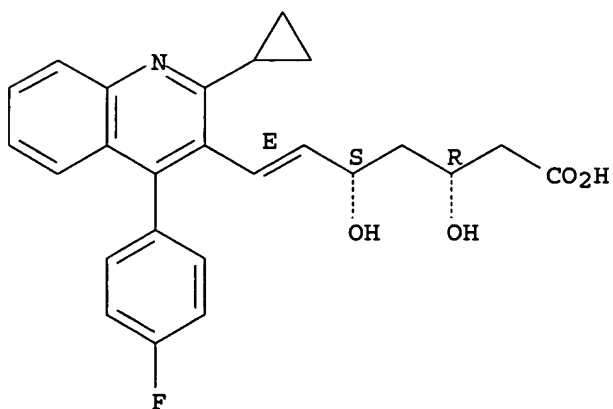
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with (αR)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1

CMF C25 H24 F N O4

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

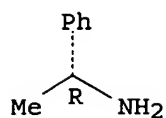


CM 2

CRN 3886-69-9

CMF C8 H11 N

Absolute stereochemistry.



IT 147511-71-5P 147511-72-6P 147526-32-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 147511-71-5 HCAPLUS

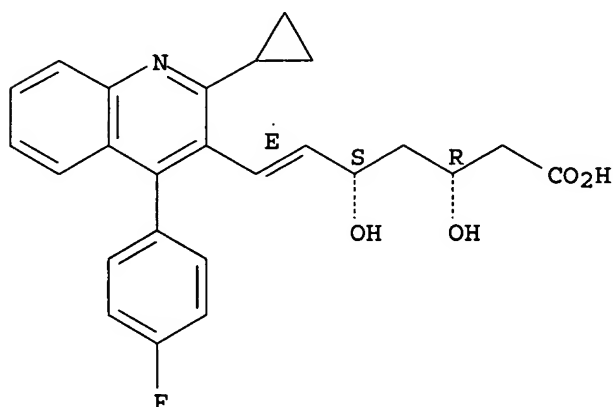
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, [S-[R*,S*-(E)]]-, compd. with (R)- α ,4-dimethylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1

CMF C25 H24 F N O4

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

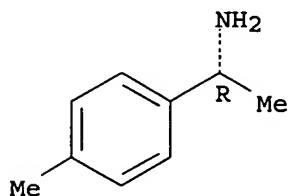


CM 2

CRN 4187-38-6

CMF C9 H13 N

Absolute stereochemistry. Rotation (+).



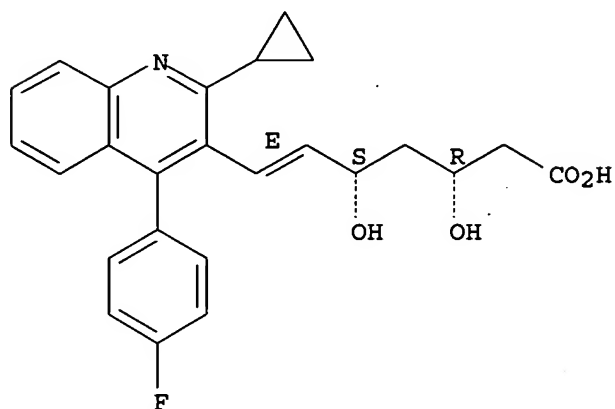
RN 147511-72-6 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, [S-[R*,S*-(E)]]-, compd. with (R)-2-amino-1-butanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1
CMF C25 H24 F N O4

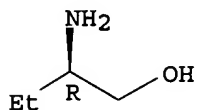
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

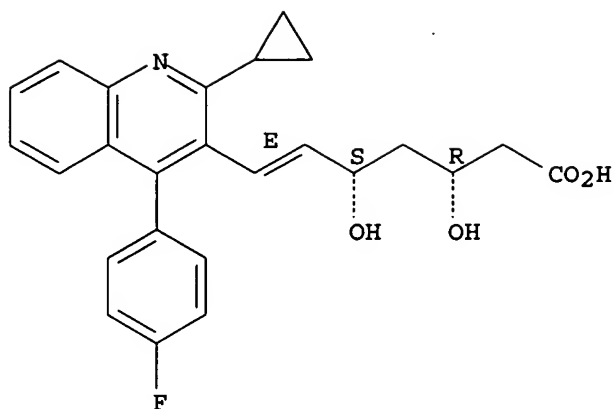
CRN 5856-63-3
CMF C4 H11 N O

Absolute stereochemistry. Rotation (-).



RN 147526-32-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



● 1/2 Ca

IT 147008-20-6

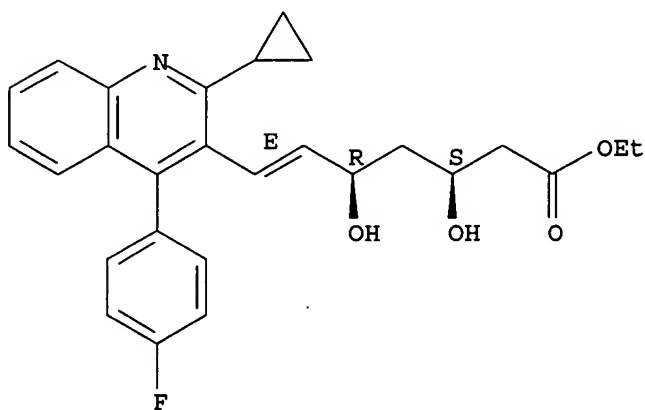
RL: RCT (Reactant); RACT (Reactant or reagent)
(saponification of)

RN 147008-20-6 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.



L67 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:407804 HCAPLUS

DN 117:7804

TI Optically active esters of 7-substituted 3,5-difunctionalized 6-heptenoic acids

IN Hiyama, Tamejiro; Minami, Tatsuya; Hanamoto, Takeshi; Reddy, Guntoori Bhaskar

PA Sagami Chemical Research Center, Japan

SO Eur. Pat. Appl., 34 pp.

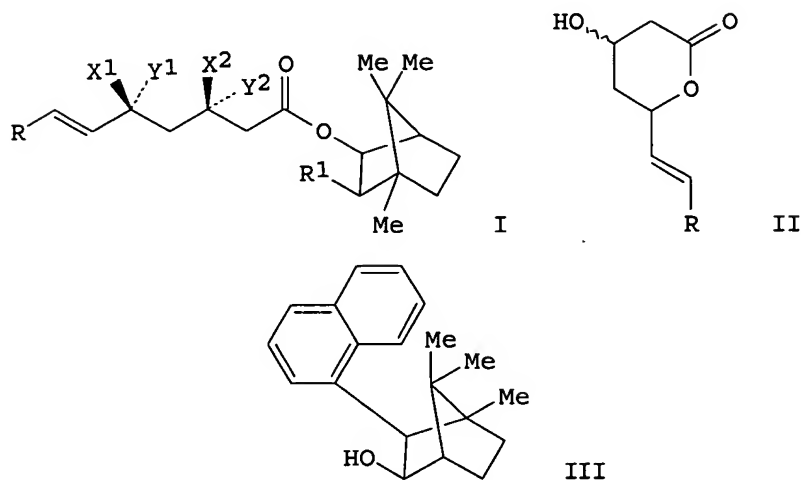
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 475627	A1	19920318	EP 1991-307837	19910828 <--
	EP 475627	B1	19941019		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05004943	A2	19930114	JP 1991-214148	19910801 <--
	US 5276154	A	19940104	US 1991-748076	19910821 <--
	HU 58267	A2	19920228	HU 1991-2818	19910829 <--
	HU 209583	B	19940829		
	CA 2050266	AA	19920301	CA 1991-2050266	19910829 <--
	US 5369109	A	19941129	US 1993-77454	19930617 <--
	PRAI JP 1990-226741		19900830 <--		
	JP 1991-214148		19910801 <--		
	US 1991-748076		19910821 <--		
OS	MARPAT 117:7804				
GI					



AB Title esters I [R = (un)substituted aromatic, heteroarom., substituted vinyl; R1 = condensed aromatic; X1 = H, Y1 = OH, X1 = OH, Y1 = H, X1Y1 = O; X2 = H, Y2 = OH, X2 = OH, Y2 = H, X2Y2 = O] were prepared as intermediates for the HMG-CoA reductase-inhibiting heptenolides II. Thus, (-)-camphor was converted to the alc. III in 5 steps. III was converted to its acetoacetate and heated with (E)-PhCH:CHCONMeOMe to give I (R = Ph, R1 = 1-naphthyl, X1Y1, X2Y2 = O). The latter compound was reduced by MeOBET2 to I (R = Ph, R1 = 1-naphthyl, X1, X2 = H, Y1, Y2 = OH) which was hydrolyzed to (3S,5R)-II (R = Ph).

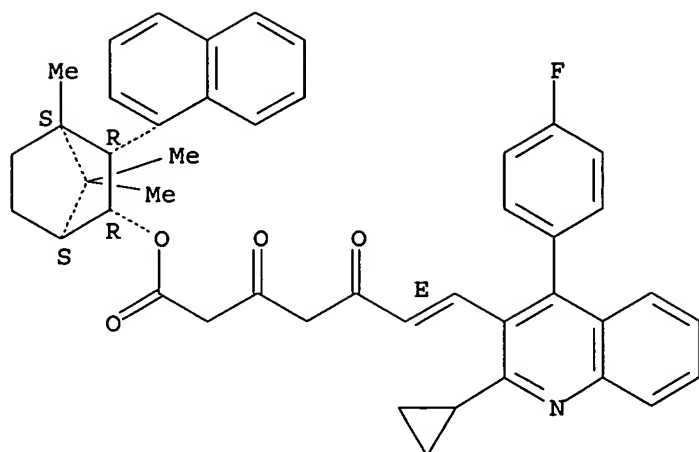
IT 141750-57-4P 141750-61-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and stereoselective reduction of)

RN 141750-57-4 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

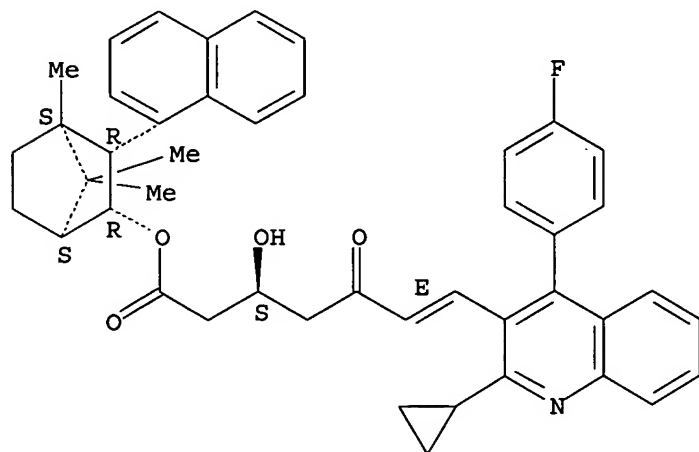
Absolute stereochemistry.
Double bond geometry as shown.



RN 141750-61-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (3R*,6E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



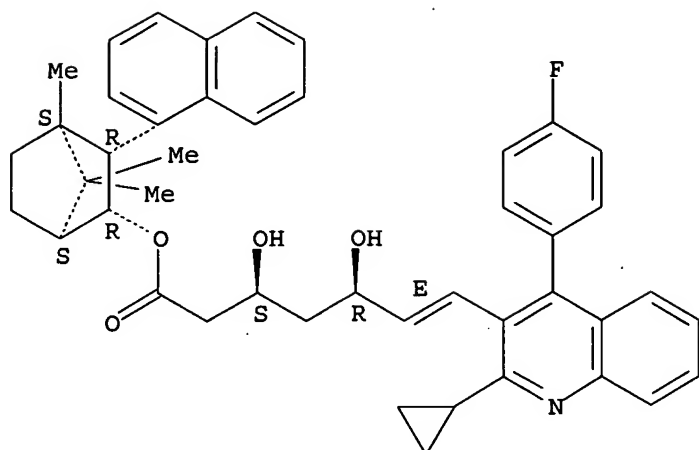
IT 141750-58-5P 141750-62-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, hydrolysis, and lactonization of)

RN 141750-58-5 HCAPLUS

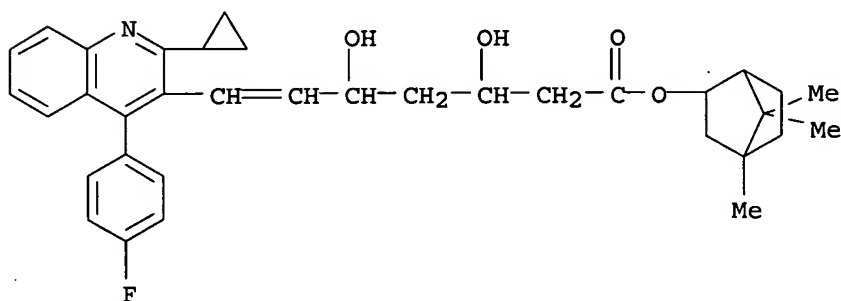
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1 α ,2 α (3R*,5S*,6E),3 α ,4 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 141750-62-1 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethylbicyclo[2.2.1]hept-2-yl ester, [1S-[1 α (3S*,5R*,6E),4 α]]- (9CI) (CA INDEX NAME)



L67 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:534010 HCAPLUS

DN 111:134010

TI Quinolinylheptenoic acid derivatives as anticholesteremics, their preparation, and formulations containing them

IN Fujikawa, Yoshihiro; Suzuki, Miki; Iwasaki, Hiroshi; Sakashita, Mitsuaki; Kitahara, Masaki

PA Nissan Chemical Industries, Ltd., Japan

SO Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

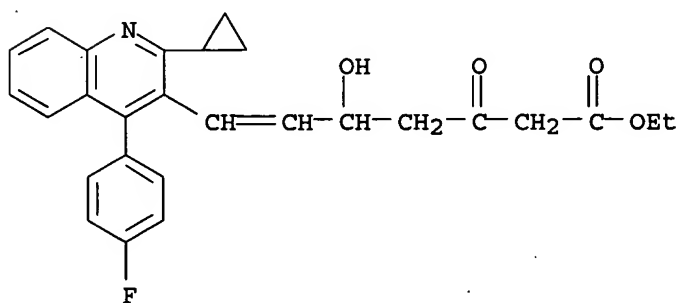
DT Patent

LA English

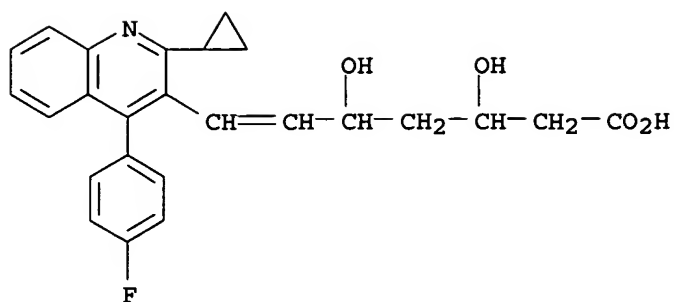
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 304063	A2	19890222	EP 1988-113448	19880818 <--
	EP 304063	A3	19901003		
	EP 304063	B1	19941130		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 01279866	A2	19891110	JP 1988-193606	19880803 <--
	JP 2569746	B2	19970108		
	CA 1336714	A1	19950815	CA 1988-574999	19880817 <--
	ES 2067460	T3	19950401	ES 1988-113448	19880818 <--
	US 5011930	A	19910430	US 1990-483720	19900223 <--

US 5102888 A 19920407 US 1990-483724 19900223 <--
 US 5185328 A 19930209 US 1990-483829 19900223 <--
 US 5872130 A 19990216 US 1990-631092 19901219 <--
 US 5856336 A 19990105 US 1992-883398 19920515 <--
 US 5854259 A 19981229 US 1992-978884 19921119 <--
 PRAI JP 1987-207224 19870820 <--
 JP 1988-15585 19880126 <--
 JP 1988-193606 19880803 <--
 US 1988-233752 19880819 <--
 US 1990-631092 19901219 <--
 US 1992-883398 19920515 <--
 OS MARPAT 111:134010
 GI For diagram(s), see printed CA Issue.
 AB The title compds. I [R1-R4, R6 = H, C1-6 alkyl, C3-6 cycloalkyl, C1-3 alkoxy, etc.; or R1 and R2, R3 and R4 may form CH:CHCH:CH, etc.; Y = CH2, CH2CH2, CH:CH, CH2CH:CH, CH:CHCH2; Z = QCH2WCH2CO2R12, Q1, etc.; Q = C(O), CH(OH), etc.; W = C(O), C(R11)(OH), etc.; R11 = H, C1-6 alkyl; R12 = H, R14; R14 = physiol. hydrolyzable alkyl, M; M = NH4, Na, K, etc.; R5 = H, C1-6 alkyl, C2-3 alkenyl, C3-6 cycloalkyl, etc.], useful as cholesterol biosynthesis inhibitors, were prepared Reduction of Et (E)-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)quinolin-3'-yl]-5-hydroxy-3-oxohept-6-enoate (preparation given) with NaBH4, followed by saponification in 0.5N NaOH, gave (E)-3,5-dihydroxy-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)-quinolin-3'-yl]-hept-6-enoic acid Na salt (II). II exhibited an IC50 of 1.0 + 10-8M against cholesterol biosynthesis from acetate in vitro. A capsule formulation containing II 1, lactose 3.5, cellulose 10, Mg stearate 0.5 g is given.
 IT 121660-87-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, in preparation of cholesterol biosynthesis inhibitor)
 RN 121660-87-5 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)

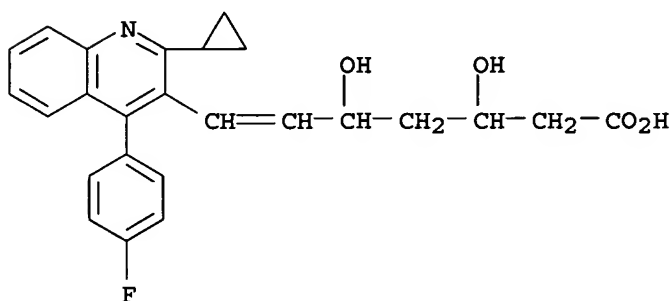


IT 121659-03-8P 121659-04-9P 121659-23-2P
 121661-13-0P 121678-77-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as cholesterol biosynthesis inhibitor)
 RN 121659-03-8 HCAPLUS
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 121659-04-9 HCAPLUS

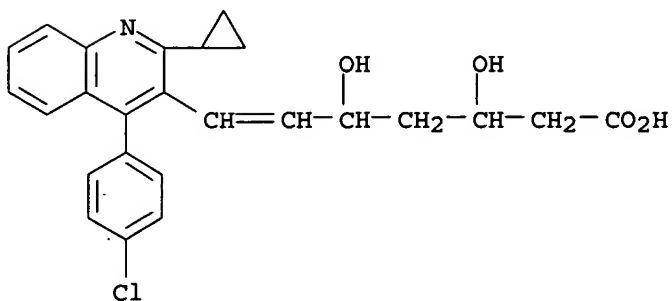
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

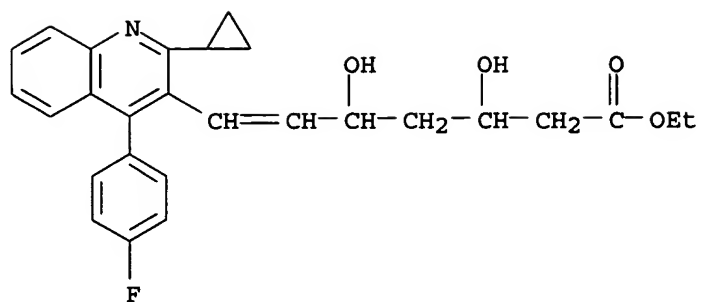
RN 121659-23-2 HCAPLUS

CN 6-Heptenoic acid, 7-[4-(4-chlorophenyl)-2-cyclopropyl-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



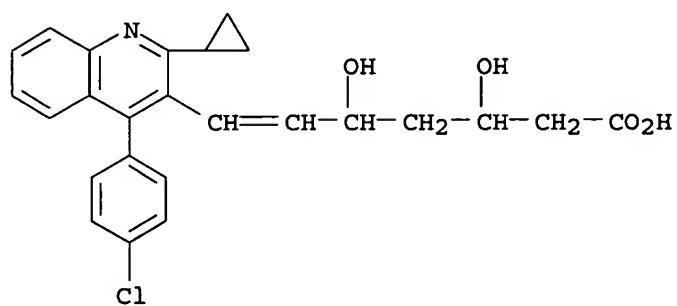
RN 121661-13-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 121678-77-1 HCAPLUS

CN 6-Heptenoic acid, 7-[4-(4-chlorophenyl)-2-cyclopropyl-3-quinolinyl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

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